TOTAL-BODY CT SCANNING IN TRAUMA PATIENTS

BENEFITS AND BOUNDARIES

Joanne Sierink

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GENERAL INTRODUCTION AND OUTLINE OF THE THESIS

GENERAL INTRODUCTION

Trauma is the third cause of death across all age groups (after cardiovascular diseases and cancer), but it is the number one cause in North Americans aged between 1 and 44 years.[1] Every two minutes one European citizen dies of a traumatic injury.[2] Many others are disabled by accidents or violence. Since most trauma patients are in their working-age years, the economic burden is reflected not only by health care costs, but also in lost productivity. When inital trauma care can be improved, lives might be saved.

The origin of protocollized trauma work-up lies in the late seventies when James K. Styner, an orthopedic surgeon, crashed his plane into rural Nebraska.[3] His wife was killed instantly. Three of his four children were severely injured and he was appalled by the abominable care they received in the local hospital. Various medical and nursing groups began to work together to provide a protocol for the management of severely injured patients. The American College of Surgeons modified the set of protocols into the first Advanced Trauma Life Support (ATLS) book, published in 1980.[4] Currently, the ATLS® course is used worldwide to train docters in the primary management of trauma victims, whether they are admitted to a rural hospital with limited resources or to an academic level-1 trauma center with a broad range of diagnostic and management possibilities.

In-hospital trauma evaluation

The ATLS® course is based upon the principle 'treat first what kills first'.[4] Protocollized clinical examination and diagnostic tests are performed and the trauma patient is managed by a multidisciplinary team of surgeons, anesthesiologists and radiologists. The primary survey consists of an ABCDE approach, an acronym for Airway, Breathing, Circulation, Disability and Exposure. When vital functions are normal or stabilized the secondary survey follows, which consists of a complete head to toe examination supplemented by radiological imaging and other adjuncts.
The past decades, there has been a major shift in the trauma care setting. First, specialized care in designated trauma centers has improved trauma outcome.[5,6] Secondly, clinically relevant time intervals are more often used as a quality indicator, although there is no scientific evidence to support the correlation between time intervals and quality of care.[7-9] Lastly, the Computed Tomography (CT) scan has established its crucial role as a supplemental tool to conventional radiologic imaging or even as its replacement during trauma survey.

Conventional radiological imaging and selective CT scanning

Conventional radiological imaging of severely injured patients routinely consists of plain X-rays of the chest and pelvis. Ultrasound of the abdomen is done by Focussed Assessment of Sonography for Trauma (FAST), which is used as a rapid screening tool for the presence of intra-abdominal and intrapericardial fluid.[10,11] Since 2009, the Eastern Association for the Surgery of Trauma

(EAST) in the United States, advocates CT scanning of the cervical spine as a replacement for cervical X-rays.[12] The clinical decision to perform imaging of the cervical spine, is based upon the Nexus criteria or Canadian C-spine rules.[13,14] Recently, the current standard of care for imaging of the thoracolumbar spine (TLS) is also redefined in an EAST guideline and CT scanning is recommended as the screening modality of choice.[15] In general, TLS imaging is performed when there is a clinical suspicion for spine injuries or when there is a trauma mechanism prone to injuries of the thoracolumbar spine (e.g. axial trauma).

Plain X-rays are widely available, have a high specificity for the detection of fractures and are relatively inexpensive. Radiation doses of plain X-rays expressed in milliSievert (mSv) are negligible compared to CT (eg. a posteroanterior chest X-ray is 0.02mSv and an adult chest CT is 5mSv).[16] However, the sensitivity of plain X-rays for the detection of severe injuries is low. For example, chest X-ray has a sensitivity ranging from 10-45% for the detection of a pneumothorax and about 50% for the detection of rib fractures[17]. The sensitivity of a pelvic X-ray for the detection of significant pelvic fractures varies between 50-70%.[18-22]

In the past decades, CT scanning is increasingly used in the assesment of trauma patients.[23-26] Primarily, selective CT scans of certain body regions were performed as a supplement to conventional imaging. CT scanners became faster, more detailed and more available in the trauma care setting. Since the introduction of the multidetector-row technology in the 1990s, CT scanning has been used more often as a replacement for conventional imaging.[27] Image quality was further refined by investigating different patterns of intraveneous contrast infusion[28]. Furthermore, it was shown that image quality could be increased by repositioning the patient with his arms raised beside the head.[29,30]

CT has a high sensitivity for the detection of injuries to most body regions.[31-34] For example, CT images greatly improve the detection of thoracic injuries and in 20% will reveal more extensive injuries compared with abnormal plain radiographs, necessitating a change of management.[35] CT scanning is also valuable for the diagnosis of abdominal injuries and proved to perfectly identify patients with active bleeding or bowel, mesenteric or pancreatic injuries.[36]

It was shown that the location of the CT scanner in or near the trauma room, as opposed to at the Radiology Department, could also have a beneficial effect on outcome.[37,38] A higher availability of the CT scanner in the trauma room facilitates its routine use.[39] The Nijmegen trauma research group performed a study to compare routine CT scanning of the chest and abdomen with a selective CT algorithm in severely injured patients. It was shown that with a routinely performed CT scan of the chest, in almost 10 percent of the patients additional injuries were found that led to a change of treatment.[40] For the routine CT scan of the abdomen this percentage was about 6 percent.[41]

Despite its favorable characteristics, CT scanning is still associated with a high radiation dose[42,43] and might affect health care costs.[44]

Total-body CT scanning

A landmark article on the role of total-body CT (TBCT) scanning in trauma patients was published by Huber-Wagner and colleagues in 2009.[45] This retrospective analysis of a subset of data (2002-2004) from the German Trauma Registry showed an increase in the probability of survival in patients who received a total-body CT scan (n=1494) compared to those who received no CT scan at all or a selective CT scan (n=3127). The authors conclude that "Total-body CT is recommended as a standard diagnostic method during the early resuscitation phase for patients with polytrauma." The results may however be confounded by the so called 'immortal time bias'.[46] This means that patients that were included in the TBCT cohort, had to survive until the scan was completed. Subsequently, the patients who died before the scan was performed were assigned to the non-TBCT cohort, which might overestimate the number of fatal events in the non-TBCT cohort. Secondly, there were no differences in crude mortality rates found between the TBCT and control group, but CT scanning was associated with a favorable difference between expected and observed deaths. Given the fact that TBCT scanning detects more injuries than a standard imaging strategy, the subsequently increased Injury Severity Score (ISS) and Trauma-ISS (TRISS)[47] might have artificially increased the survival rate of patients with an apparently poorer probability of survival[48].

Several retrospective and prospective studies followed this landmark study, all together assessed in six systematic reviews.[49-54] In summary, all reviews agreed on a time benefit in favor of TBCT scanning, but no consensus was obtained regarding a possible survival benefit. All systematic reviews concluded their manuscript with saying that solid scientific evidence is needed. Despite the lack of proper scientific evidence, there are more and more trauma centers that use a TBCT scan during trauma survey, either as a supplement to or as a replacement for conventional imaging.[31,55-57]

With the increased use of CT scanning, incidental (trauma-unrelated) findings are also detected more often. Incidence numbers are found to be around 50% for either selective or TBCT scanning.[58-61] In previous studies, indications for a TBCT scan were not clearly described and the clinical consequences of the incidental findings are unclear.[60,61] Incidental findings might result in increased patients' anxiety and health care costs in case of additional work-up for abnormalities that ultimately might not affect patients' health. Therefore, it is useful to know the clinical consequences of the incidental findings in a well-defined study population.

Lastly, several studies have compared radiation doses between pre- and post-total-body CT scan protocol cohorts.[23,42,43] However, in all these studies the number of polytrauma patients (Injury Severity Score ≥16) was relatively low, while this is the population we are most interested in with regard to radiation dose.[23,43,62]

OUTLINE OF THE THESIS

The aim of this thesis was to clarify the role of immediate TBCT scanning in severely injured patients, considering its benefits and boundaries. Therefore, this thesis is divided into 8 chapters.

Chapter 1 provides a systematic review of the literature regarding TBCT scanning in trauma patients. Clinical relevant time intervals were assessed, but moreover patient outcome in terms of mortality was described. If time intervals are used to determine quality of care, it is relevant to know how reliable those intervals can be measured.

Chapter 2 contains a study on the topic of clinically relevant time intervals in trauma care in a convenience sample of 100 patients. Subsequently we were interested in which TBCT scanning protocol would suit best for the detection of injuries in trauma patients.

In **Chapter 3** we describe a prospective pilot study in which three different TBCT scanning protocols are compared with regard to optimal image quality. Three radiologists independently evaluated protocol quality scores, parenchymal and vascular enhancement and artifacts.

In **Chapter 4** a historical cohort of patients who underwent immediate TBCT scanning, without previous conventional imaging, was case-matched with patients who underwent conventional imaging supplemented by selective CT scanning. Groups were compared with regard to thirty-day mortality.

Chapter 5 shows an overview of incidental (eg. trauma-unrelated) findings accompanied by TBCT scanning.

Chapter 6 examines the amount of radiation exposure that polytrauma patients (i.e. ISS≥16) were exposed to before and after the introduction of a dedicated total-body CT scan protocol.

Chapter 7 comprises the study protocol of the Randomized clinical trial of Early Assessment with CT scanning in trauma patients (REACT-2) study. The REACT-2 trial is the first randomized clinical trial on this topic worldwide. Trauma patients are randomized to either conventional imaging with X-rays and FAST, supplemented by a selective CT scan, or to an immediate TBCT scan. In this chapter background, eligible patients and (statistical) methods are described extensively.

Lastly, in **Chapter 8** the results of the REACT-2 study are presented. Results regarding the primary outcome measure (in-hospital mortality) are described as well as the most relevant secondary outcome measures (clinically relevant time intervals, radiation dose and cost-utility analysis).

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SYSTEMATIC REVIEW AND META-ANALYSIS OF IMMEDIATE TOTAL-BODY COMPUTED TOMOGRAPHY COMPARED WITH SELECTIVE RADIOLOGICAL IMAGING OF INJURED PATIENTS

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ABSTRACT

Objective The aim of this review was to assess the value of immediate total-body computed tomography (CT) during the primary survey of injured patients compared with conventional radiographic imaging supplemented with selective CT.

Methods A systematic search of the literature was performed in MEDLINE, Embase, Web of Science and Cochrane Library databases. Reports were eligible if they contained original data comparing immediate total-body CT with conventional imaging supplemented with selective CT in injured patients. The main outcomes of interest were overall mortality and time in the emergency room (ER).

Results Four studies were included describing a total of 5470 patients; one study provided 4621 patients (84.5 percent). All four studies were non-randomized cohort studies with retrospective data collection. Mortality was reported in three studies. Absolute mortality rates differed substantially between studies, but within studies mortality rates were comparable between immediate total-body CT and conventional imaging strategies (pooled odds ratio 0.91, 95 percent confidence interval 0.79 to 1.05). Time in the ER was described in three studies. In two it was significantly shorter in patients who underwent immediate total-body CT: 70 vs.104 min ($P = 0.025$) and 47 vs. 82 min ($P < 0.001$) respectively.

Conclusion This review showed differences in time in the ER in favour of immediate total-body CT during the primary trauma survey compared with conventional radiographic imaging supplemented with selective CT. There were no differences in mortality. The substantial reduction in time in the ER is a promising feature of immediate total-body CT, but well designed and larger randomized studies are needed to see how this will translate into clinical outcomes.

INTRODUCTION

The initial diagnostic evaluation of injured patients is frequently based on Advanced Trauma Life Support (ATLS®) principles, including a fast and priority-based physical examination as well as screening radiographs supplemented with selective computed tomography (CT).[1] Since the introduction of spiral CT in the early 1990s[2], CT scanning has become more important in trauma care.

The introduction of multi-detector-CT (MDCT) scanners made total body CT (TBCT) technically feasible and its high diagnostic accuracy makes it an attractive diagnostic tool for the initial radiographic imaging of trauma patients. [3-5] Furthermore, the amount of scanning time needed to obtain a TBCT appears to be acceptable.[4,6-10] An increasing number of trauma centers encourages the use of immediate TBCT in the diagnostic phase of primary trauma care.[4,11-19] The number of time-consuming transfers (and associated dangers) will be decreased with the use of immediate total-body CT. Furthermore, rapid total-body CT in an environment that enables resuscitation may streamline clinical pathways. Whether the advantages of such scanning justify the higher radiation dose given remains controversial. [15,20,21] The most important remaining question is whether the use of immediate TBCT improves survival.

The primary aim of this systematic review was to assess whether immediate TBCT scanning during primary survey is associated with a lower mortality than conventional imaging supplemented with CT scanning. The second goal was to determine its effect on the time in the emergency room (ER).

MATERIALS AND METHODS

The guidelines for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were followed.[22]

In- and exclusion criteria

Studies comparing immediate total-body CT during the primary survey of injured patients with conventional imaging and selective CT in a control group were included. Methods of analysis and inclusion criteria were specified in advance. Both randomized and observational studies were included. Only studies with a mainly adult study population were included (defined as median age of the study group above 16 years). Case reports, reviews, editorials, meeting abstracts and theses were excluded. Publications in a language other than English or German were also excluded.

Outcome

The main outcome of interest was overall mortality rate. The secondary outcome measure was time spent in the ER. Missed injury rates, complications and total length of hospital stay were also analyzed.

Search strategy

The MEDLINE, Embase Web of Science and Cochrane Library databases were searched for articles published between 1947 and November 2010 (cut-off date 1 November 2010). The search terms consisted of [['fbct' or 'tbct' or 'whole body ct' or 'total body ct' or 'full body ct'] OR ['whole body' or 'full body' or 'total body'] AND ['ct' and 'scan*' or 'tomograph*' or 'ct scan']]. These terms were combined with the following terms: ['trauma' or 'injur*' or 'shock*' or 'emergen*'].

In addition, reference lists of each eligible article and reviews selected for abstract screening were scanned for additional references. The last search was performed in October 2010 and was conducted with the help of a clinical librarian.

Study selection

Two reviewers independently assessed titles or abstracts of all studies identified by the initial search and excluded irrelevant studies. The full text of potentially relevant studies was obtained. Then full-text articles were assessed to determine whether they met the inclusion criteria for this review. Any discrepancies in inclusion were resolved by discussion between the reviewers. If necessary, an independent third reviewer was consulted.

Data extraction and methodological quality

Two reviewers extracted the following data from each included paper on a data extraction sheet: publication year, sample size, language in which the paper was written, study design, patient characteristics, type of intervention and outcomes. Disagreements were resolved by discussion between the two reviewers; if no agreement could be reached, a third reviewer made the final decision. Furthermore, the corresponding author of an original study was contacted if the reported data were unclear or incomplete.

The methodological quality of the studies was described using the Newcastle–Ottawa Scale, designed for assessing the quality of non-randomized studies in meta-analyses. It scores potential sources of bias and variation in cohort studies regarding selection, comparability and outcome.[23]

Statistical analysis

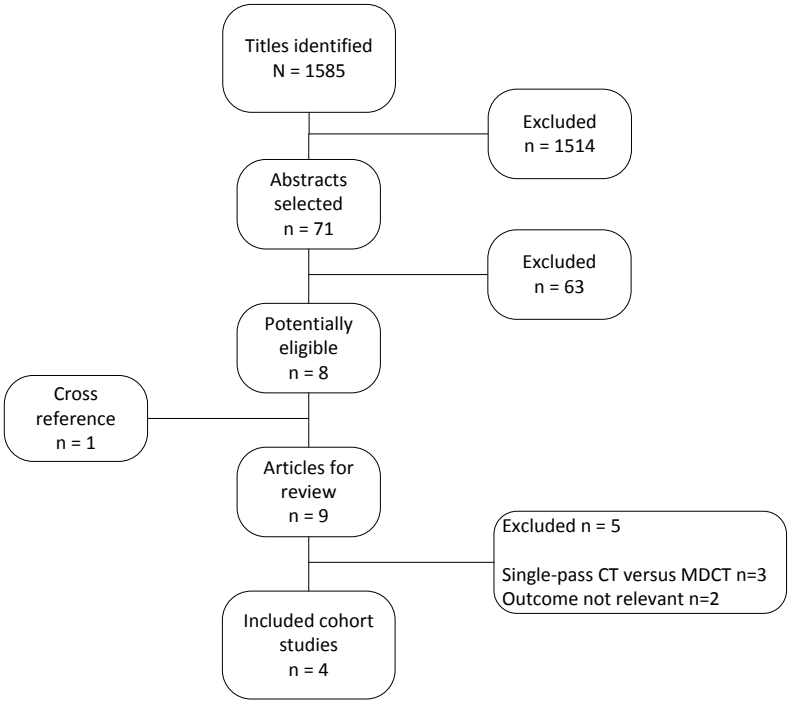
Patient characteristics, mortality rates and time in the ER for each included study were summarized using descriptive statistics. For mortality, data were extracted to calculate the odds ratio and its standard error for each study. Random-effects meta-analysis of the logit-transformed proportion of mortality was done using the NLMIXED procedure (non-linear mixed model) (SAS® version 9.2; SAS Institute, Cary, North Carolina, USA).

RESULTS

Search strategy and selection

The computerized search resulted in 796 titles from the MEDLINE database, 396 titles from the EMBASE database, 382 from the Web of Science database and 11 titles from the Cochrane database. Following application of inclusion and exclusion criteria, eight full-text articles were reviewed (Figure 1). The cross-reference search added one additional paper, giving a total of 9 articles for full-text review. [6,13,15,20,24-28] Five of these were found to be irrelevant to this systematic review (three made a comparison between single-pass TBCT and multi-detector TBCT; two had irrelevant outcomes).[6,13,15,20,24] Therefore, the remaining four studies were included. [25-28]

Figure 1 Flow chart for the review.



Abbreviations: CT, computed tomography; MDCT, multidetector CT.

These studies all had a non-randomized cohort design with retrospective data collection. They reported on mortality as well as time in the ER[26], mortality and time to the operating room[28], mortality alone[25] and time in the ER alone.[27] Huber-Wagner and colleagues[25] were contacted and provided additional information on time in the ER. Wurmb and co-investigators[27, 28] provided their raw data with mean ISS scores.

The included studies scored 6 or more (maximum 8) on the Newcastle-Ottawa scale. All studies achieved the maximum amount of points regarding the 'selection' category. Comparability of the cohorts was not always assured because three of the studies did not adjust for possible confounders in the analysis. Outcome was generally recorded well, although most of the studies made no comments regarding the follow-up time. Furthermore, all included studies lacked randomization, a power calculation, long-term mortality reports and quality-of-life data. None of the studies was excluded because of poor methodological quality. The level of evidence was 2b according to the Oxford Level of Evidence scale.[29]

Data extraction

The four studies described a total of 5470 patients.[25-28] One series, with a population of 4621, provided 84.5 percent of the total number of patients.[25] The median sample size of the other three studies was 318. The study characteristics are summarized in Table 1. All reports provided data on the comparison between injured patients analyzed by immediate total-body CT and a control group that had conventional imaging supplemented with CT.

Table 1 Characteristics of the four eligible studies

Reference	Year	Country	Study design	Newcastle-Ottawa scale	N
Huber-Wagner[25]	2009	Germany, Austria and Switzerland	Non-randomized cohort	7 of 8	4621
Weninger[26]	2007	Austria	Non-randomized cohort	7 of 8	370
Wurmb[27]	2009	Germany	Non-randomized cohort	6 of 8	161
Wurmb[28]	2011	Germany	Non-randomized cohort	7 of 8	318

Total-body CT was performed with MDCT scanners, and comprised unenhanced imaging of the head followed by contrast-enhanced CT of the chest, abdomen and pelvis. The scanner was located in the ER in three studies, whereas information on its location was not available in one report.[25] In three studies a 16-slice MDCT instrument was used; one multicenter study provided no information about the scanners.[25] The scanning protocols for CT, when described,

varied regarding the slice thickness, which ranged from 0.75 to 5 mm for the head and neck, and from 1 to 5 mm for the torso. Detailed information on rotation time, table speed and delay after injection of contrast material was not described routinely. Variations were also seen in the workflow; some centers performed focussed assessment with sonography for trauma (FAST) in hemodynamically unstable patients to examine the abdomen for the presence of free fluid before starting total-body CT. Conventional evaluation strategies were not described routinely in each study, but in general consisted of plain X-ray of the chest, cervical spine and pelvis, a check of the abdomen by FAST and, finally, selective CT when necessary.

Table 2 Patient demographics

Reference	N	Trauma mechanism	Mean age (years)			Median ISS (points)		
			Total-body CT	Conventional imaging	P-value	Total-body CT	Conventional imaging	P-value
Huber-Wagner[25]	4621	blunt	42.5	42.7	0.85	32.4*	28.4*	<0.001
Weninger[26]	370	blunt	43.5	40.7	nsˆ	26.6*	27.6*	nsˆ
Wurmb[27]	161	blunt	39	36	nsˆ	24	22	nsˆ
Wurmb[28]	318	blunt and penetrating	38	38	nsˆ	27	24	0.001

Abbreviations: ISS, Injury Severity Score; NS, not significant. *Values are mean. Conventional imaging comprised conventional imaging strategies supplemented with selective computed tomography (CT).

Table 2 shows the demographics of the study groups. Three studies included only patients with blunt trauma[25-27], and one also included patients with penetrating trauma.[28] The mean age varied from 36 to 44 years, and did not differ significantly between the total-body CT and control groups in any of the studies. In two studies, the Injury Severity Score (ISS) was comparable between the two groups[26;27], whereas in the other two series patients who received immediate total-body CT had a significantly higher ISS.[25;28] One study included only patients who underwent emergency surgery immediately after trauma resuscitation and diagnosis in the trauma room.[28]

Data on outcome are summarized in Table 3. Mortality was reported in three studies.[25;26;28] Huber-Wagner and colleagues[25] described an overall mortality rate of 20.5 percent among patients who had total-body CT versus 22.1 percent in the group evaluated with conventional imaging strategies (P = 0.21). Weninger et al.[26] reported similar in-hospital mortality rates in the two groups (16.2 versus 16.8 percent), and Wurmb *et al.*[28] found no significant difference in 30-day mortality rates (8.6 versus 9.0 percent). The absolute mortality rates varied widely between studies. Within studies, however, mortality rates were comparable between immediate total-body CT and conventional imaging strategies (pooled odds ratio 0.91, 95 percent confidence interval 0.79 to 1.05) (Figure 2). The result was the same when patients with an ISS of 0–15 in one study[28] were excluded (pooled odds ratio 0.91, 0.78 to 1.05).[25;26;28]

Table 3 Outcomes

	Median time in ER (min)			Overall mortality (%)		
Reference	Total-body CT	Conventional imaging	P-value	Total-body CT	Conventional imaging	P-value
Huber-Wagner[25]	70* (tER)	78* (tER)	nsˆ	21%	22%	0.21
Weninger[26]	70 (tER)	104 (tER)	0.025	16%‡	17%‡	nsˆ
Wurmb[27]	47 (tER)	82 (tER)	<0.001	na	na	-
Wurmb[28]	105 (tOR)	120 (tOR)	<0.05	8.5%▪	9%▪	nsˆ

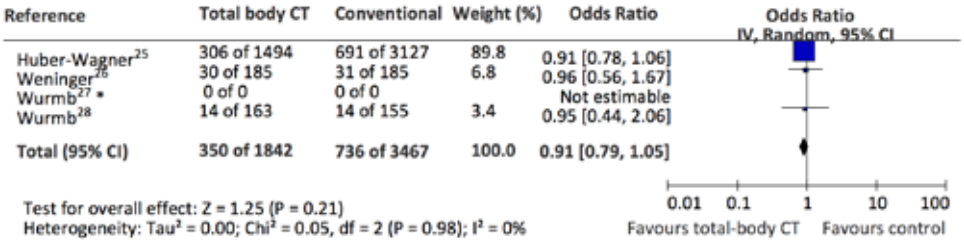
Abbreviations: Total-body CT, total body computed tomography; Conventional imaging, conventional imaging strategies supplemented with selective CT; tER, time in the emergency room; tOR, time to the operating room; ISS, injury severity score; na, not available; ns, not significant. * mean, ˆ P-value not mentioned, ‡ in-hospital mortality rate, ▪ 30-day mortality rate

Time in the ER was registered in three studies.[25-27] Huber-Wagner and colleagues (personal communication) reported no difference between the total-body CT and conventional imaging groups (70 versus 78 min respectively), whereas time in the ER was significantly shorter in the immediate total-body CT group in the studies by Weninger et al. [26] (70 versus 104 min; P = 0.025) and Wurmb and co-workers[27] (47 versus 82 min; P < 0.001). One study reported time

to the operating room, which was significantly shorter among patients who had total-body CT (105 versus 120 min; P < 0.050).[28]

None of the included studies described missed injury or complication rates. Total length of hospital stay was described in two studies. Huber-Wagner and colleagues[31] reported a mean hospital stay of 28.2 days in the total-body CT group versus 25.0 days in the conventional group (P = 0.002), whereas Weninger and co-workers[26] reported 29.0 and 32.5 days respectively (P = 0.046).

Figure 2 Meta-analysis of overall mortality.



A random-effects model was used. Odds ratios are shown with 95 percent confidence intervals on a logarithmic scale. * No mortality data reported.

DISCUSSION

Mortality rates did not differ between patients who were evaluated with immediate total-body CT and those who had conventional imaging supplemented by selective CT. However, the studies differed markedly in their absolute mortality rates and the meta-analysis was dominated by one large study.[25] Time in the ER, registered in three studies, was significantly shorter in patients who underwent immediate total-body CT in two studies and showed a non-significant difference in favor of this approach in the third report. Missed injury and complication rates were not described in the included studies. Although two studies described a significant difference in length of hospital stay between the groups, these results were inconclusive.

All reviewed studies had a retrospective non-randomized design. Because of their retrospective nature, they showed associations rather than causalities. Characteristics of included injured patients, especially ISS, determined prognosis and this could have caused selection bias. Wurmb and colleagues[27;28], for example, included patients with an ISS of 0–15, which probably accounted for the lower mortality rates in their studies compared with the other series. However, reanalysis of the original data from Wurmb *et al.*[27;28], after exclusion of patients with an ISS of 0–15, showed a mean ISS and trends in outcome variables comparable with those of the other studies (data not shown).

Differences in time in the ER between the two groups may have depended on factors other than the one under study. Selection bias among patients subjected to total-body CT and CT protocols (arm-raising before contrast-enhanced CT of the torso is time-consuming) may have affected the measured time intervals. The experience of the trauma team, imaging interpretation by the radiologist and different institutional levels may also have played a role. The indications for CT were well defined in most reports, but in one study the indications were chosen by each participating hospital and were not mentioned separately.[25]

Overall, the smaller number of cohort studies identified, the small sample sizes (with the exception of one study) and the many differences in study protocols and methods hampered interpretation of the results. Several studies reported data on time factors related to the use of immediate total-body CT, but fewer studies compared the effects of immediate total-body CT *versus* conventional imaging supplemented with selective CT. Even less is known about the effects on survival.

Injured patients are exposed to significant radiation doses during diagnostic imaging with total-body CT.[21] The effective radiation dose is assumed to be 10–20 mSv for one examination.[30] However, conventional imaging protocols supplemented with CT account for significant radiation doses as well[31], and so the burden in terms of radiation dose of immediate total-body CT remains controversial.[15;20;21]

Although immediate total-body CT has proved to be highly accurate in detecting a range of significant injuries[3;4;6-9;14;32], its effect on clinical outcome remains unclear. Some studies have suggested a trend towards lower mortality when immediate total-body CT is used. In the large study by Huber-Wagner and colleagues[25] the patients in the total-body CT group had a significantly higher ISS than those in the control group. Despite this unfavorable prognostic characteristic, mortality rates were comparable with those among less severely injured patients who underwent conventional imaging. However, it is uncertain whether this was a consequence of use of the total-body scan. Furthermore, the same study reported a significant increase in probability of survival for patients who had immediate total-body CT compared with those who underwent non-total-body CT.[25] Hilbert and co-workers[18] described a decrease in mortality rate from 15 to 8.6 percent after introduction of a clinical algorithm using immediate total-body CT in the clinical care of seriously injured patients. Whether this was due to the scan or to the clinical care algorithm, and whether the study groups were comparable, remains unclear.

Larger and higher-quality studies are needed to further examine the potential role and value of immediate total-body CT in the primary trauma survey.[33] Future studies should randomize patients with comparable prognosis to either immediate total-body CT in the trauma room or conventional imaging supplemented with selective CT. It is crucial to select patients who will benefit the most from immediate total-body CT. Outcomes of interest are (24-h or in-

hospital) mortality, several clinical relevant time intervals, missed injuries, complication rates, radiation exposure during the hospital stay and cost-effectiveness of the intervention in both cohorts. For the CT protocol, use of a MDCT scanner is mandatory and availability of multiplanar reconstructions is strongly recommended. The direct evaluation and structured reporting of images by the radiologist should be guaranteed. To equalize study protocols and increase the study population, a multicenter and international study design is preferable.

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2

ROUTINELY RECORDED VERSUS DEDICATED TIME REGISTRATIONS DURING TRAUMA WORK-UP

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ABSTRACT

Objective Since time intervals are used to determine quality of trauma care, it is relevant to know how reliable those intervals can be measured. The aim of our study is to assess the reliability of time intervals as recorded in our hospital databases.

Methods We conducted a prospective study on time intervals in our level-1 trauma center and compared those with the routinely recorded data from February 2012 to June 2012. A convenience sample of all trauma patients admitted to our trauma room was included. The routinely recorded time intervals were retrieved from computerized hospital databases. The dedicated time registration was done on a standardized form on which five time intervals considered clinically relevant were evaluated for each patient by a dedicated person: trauma room time, time to start CT, imaging time, time from trauma room to ICU and time from trauma room to intervention.

Results In a sample of 100 trauma patients dedicated registered trauma room time was median 47 minutes (IQR = 32-63), compared to 42 minutes (IQR = 28-56) in routinely recorded time intervals ($P < 0.001$). Time to start of CT scanning differed significantly as well, with again an increased time interval measured dedicatedly (median 20 minutes (IQR = 15-28)) compared to the routinely recorded time registration (median 13 minutes (IQR = 4-21)). The other time intervals recorded did not differ between the dedicated and routinely recorded registration. Bland-Altman plots also showed that there is considerable discrepancy between the two measurement methods with wide limits of agreement.

Conclusion This study shows that routinely recorded time intervals in the trauma care setting differ statistically significant from dedicatedly registered intervals.

INTRODUCTION

Time is one of the important issues in trauma and acute care surgery. Optimal pre-hospital and in-hospital time management can be of life-saving importance. Although the Golden Hour concept is based upon an expert opinion rather than solid scientific evidence[1], national trauma databases register time intervals to be able to analyze time-management in the acute trauma care setting.[2]

Time intervals are therefore also used as a quality indicator in trauma care,[3,4] although there is no high-level evidence to support the correlation between time intervals and quality of care.[5,6] Clearly defined and based on solid scientific evidence are fundamental prerequisites for useful performance indicators.[3] In the evaluation of trauma care however a wide diversity in quality indicators is used and there is no clear set of broadly accepted indicators.[3] In order to improve performance measurement by means of quality indicators, the American College of Surgeons (ACS) Committee on Trauma has set up a National Surgical Quality Improvement Program (NSQIP).[7] In the NSQIP, several time intervals, such as time to CT and time to laparotomy or craniotomy, are used as quality indicators.[7,8] If time intervals are used to determine quality of care, it is relevant to know how reliable those intervals can be measured.

In the Dutch Trauma Registry, admission time and time of departure from the trauma room are the only time points that are registered. For quality control, performance improvement and research purposes however, other clinically relevant time points can be retrieved from hospital databases. The reliability and usability of time intervals routinely recorded in several hospital databases is not clear.

Therefore, the aim of our study is to assess the reliability of time intervals as recorded in our hospital databases.

PATIENTS AND METHODS

Patient selection and setting

We conducted a prospective study on time intervals in our level-1 trauma center and compared those with the routinely recorded data from February 2012 to June 2012. A convenience sample of all trauma patients admitted to our trauma room was included. All trauma patients admitted to the trauma room during office hours were enrolled (Monday to Friday, 8 am-6 pm). Patients admitted during night and weekend shifts were occasionally enrolled, depending on the availability of the researcher. To assure that the convenience sample taken was representative for the population as a whole, baseline characteristics between in- and excluded patients were compared.

The study setting was a level-1 trauma center in The Netherlands with approximately 750 trauma room admissions each year of which approximately 200 multi trauma patients. Trauma work-up is done according to ATLS® guidelines.[9] Radiologic imaging consists of the standard evaluation with chest and pelvic X-rays, FAST and selective CT scanning. A second trial (REACT-2) was conducted during the study period. Patients included in the REACT-2 trial are randomized between the standard evaluation and an immediate total-body CT scan.[10] A movable 64-slice CT scanner (SOMATOM Sensation 4; Siemens Medical Systems, Erlangen, Germany) is located in the trauma room.[11,12]

Definitions and time registration

Time intervals that are routinely recorded as a standard operational procedure (either fully computerized or by nursing staff) are further mentioned 'routinely recorded'. The routinely recorded time intervals were retrieved from the following databases: admission time and time of departure from the trauma room are routinely registered in the computerized hospital database by nursing staff. Start and end of radiologic imaging and time of arrival at the angiography suite are registered in a radiologic database (acquisition times of images). Time of arrival at the operating room is routinely registered by the OR nursing staff in the computerized operating report and time of arrival at the ICU is routinely registered in the computerized ICU database when a patient is connected to a ventilator or other monitoring device.

The dedicated time registration was registered on a standardized form on which the five time intervals considered clinically relevant were registered. The definitions for starting and stopping the time registration are depicted in Table 1. These definitions are based upon the routinely recorded time registration. The same definitions were used for the dedicated time registration.

Table 1 Definitions of starting and stopping time registrations

Patient leaves trauma room	Patient leaves trauma room	Patient leaves trauma room
Trauma room time	Patient enters trauma room	Patient leaves trauma room
Time to start CT	Patient enters trauma room	First CT image obtained
Imaging time	First image obtained during trauma work up	Last image obtained during trauma-workup
Time from admission on Trauma room-ICU	Patient enters trauma room	Patient arrives at the ICU
Time from admission on Trauma room-intervention*	Patient enters trauma room	Patient arrives at angio suite/OR

The definitions are based upon the routinely recorded time registration. The same definitions were used for the dedicated recorded time registration. Time registration was done by an independent researcher who was not involved in actual trauma care. Recording was started and stopped when the patient crossed the doorstep.

* Either angiographical or surgical intervention.

Time registration was done by an independent researcher who was not involved in actual trauma care. The researcher was on call during office hours (8 am to 6 pm) and occasionally during weekends and nights. Times were recorded using a smart phone with a stopwatch application. Since the times in the computerized databases are rounded to the minute, the same was done to the times measured with the stopwatch application.

Statistical analysis

All data were imported in SPSS (version 19.0; SPSS Inc, Chicago, IL). Descriptive statistics were used to describe the data. The Wilcoxon matched-pairs signed-ranks test was used to analyse the time differences between the dedicated and routinely recorded time registration. A P-value less the 0.05 is considered significant. Furthermore, the Bland-Altman plot[13] was used to assess the relative agreement between the dedicated and routinely recorded time measurements. The 'limits of agreement' are defined by Bland-Altman as the mean of the difference between the two measurement methods plus or minus 1.96 times the standard deviation of the mean.

RESULTS

In total, 338 patients were admitted to the trauma room during the study period. The analyzed convenience sample consisted of 100 trauma patients (30% of the total population admitted to the trauma room in the study period). There were no statistically significant differences found in age, sex, trauma mechanism, ISS, ICU stay and trauma-related mortality of included patients versus excluded patients, except for the length of total hospital stay (2 days (IQR = 1-7) versus 2 days (IQR = 1-5), P = 0.019).

Characteristics of the convenience sample are depicted in Table 2. Median age was 40 years, the majority of patients was male (68%) sustaining blunt trauma (97%) and median ISS was 5 (IQR = 1-13). There were 20 multi trauma patients in the convenience sample and trauma related mortality was 5%.

Table 2 Patient characteristics

	n=100
Age (years)	40.4 (IQR=22.7-66.3)
Men	68 (68%)
Blunt trauma	97 (97%)
Mechanism of injury	
fall from height	26 (26%)
motor vehicle collision	36 (36%)
bicycle accident	16 (16%)
penetrating	2 (2%)
other	20 (20%)
ISS	4.5 (IQR = 1-13)
Multitrauma patients (defined as ISS>15)	20 (20%)
Hospital stay (days)	2 (IQR = 1-7)
ICU stay (days)	2 (IQR = 1-5)
Ventilation time (days)	2 (IQR = 1-4.8)
Trauma-related mortality	5 (5%)

Data are number (%) or median (interquartile range (IQR)) unless otherwise indicated. Abbreviations: ICU= Intensive Care Unit; ISS= Injury severity score.

* Mean (SD) † Two patients had combined blunt and penetrating trauma

The dedicatedly and routinely recorded time registrations are shown in Table 3. Total trauma room time was median 47 minutes (IQR = 32-63) in the dedicated time registration and median

42 minutes (IQR = 28-56) in the routinely recorded time registration (P < 0.001). Time to start CT differed significantly as well, with again an increased time interval measured dedicatedly (median 20 minutes (IQR = 15-28)) compared to the routinely recorded time registration (median 13 minutes (IQR = 4-21)). The other time intervals recorded did not differ between the dedicated and routinely recorded registration.

Table 3 Time registration in minutes dedicatedly versus routinely recorded

	Dedicated time registration	Routinely recorded	P-value
TR time (n = 100)	46.5 (32.3-62.8)	41.5 (28–55.8)	<0.001
Time to start CT (n = 77)	20 (14.5-27.5)	13 (3.5-21)	<0.001
Imaging time (n = 100)	18 (7.3-25)	18.5 (8–25)	0.180
Time from TR to ICU (n = 21)*	56 (47.8-91.5)	58 (49.5-96)	0.410
Time from TR to intervention (n = 17)*	199 (78–261)	201 (88–256)	0.379

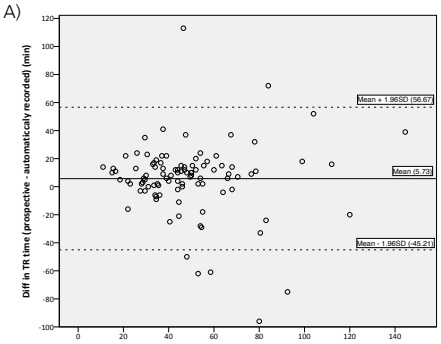
Data are number (%) or median (interquartile range (IQR)). Abbreviations: TR = trauma room; ICU = intensive care unit. Trauma Room time is time between arrival at and departure from the trauma room. *Other patients were admitted to the general ward or discharged from the ED.

Figure 1 depicts the Bland-Altman plots of the levels of agreement for the two time measurement methods. The plots showed a random nature of the spreads with biases in each plot. However, each time interval shows wide 'limits of agreement', reflected by the small sample size and great variation of the differences.[13] For example, the routinely recorded total trauma room time may be 45 minutes below or 57 minutes above the dedicatedly recorded time. Although most observations are within the limits of agreement, we assumed that the wideness of the limits would be relevant for research purposes. This was the case for time to CT as well (routinely recorded time may be 22 minutes below or 47 minutes above the dedicatedly recorded time). The range was less wide in total imaging time with 21 minutes below and 17 minutes above which might be acceptable for research purposes. For the time intervals trauma room to ICU and trauma room to intervention there were wide intervals, but those are difficult to interpret due to the small sample sizes.

Table 4 sets out the time intervals measured according to ISS. Patients with an ISS between 16 and 24 have the longest trauma room time with both measurement methods (52 minutes with the dedicated measurement and 43 minutes with the routinely recorded measurement) while patients with an ISS above 24 have the shortest time at the trauma room (44 minutes with the dedicated measurement and 38 minutes with the routinely recorded measurement).

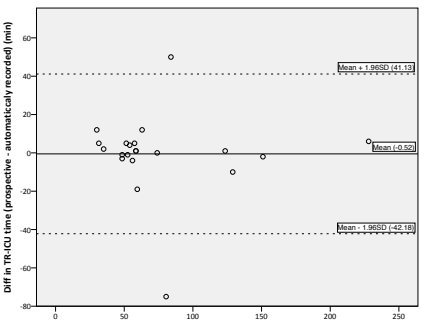
Figure 1 Bland-Altman plots (difference against mean)

A)



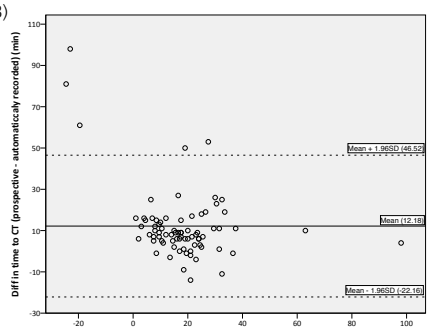
Average TR time by two measuring methods

D)



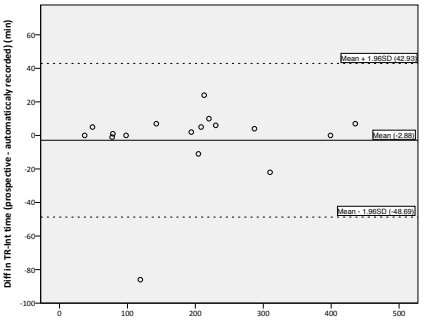
Average TR-ICU time by two measuring methods

B)



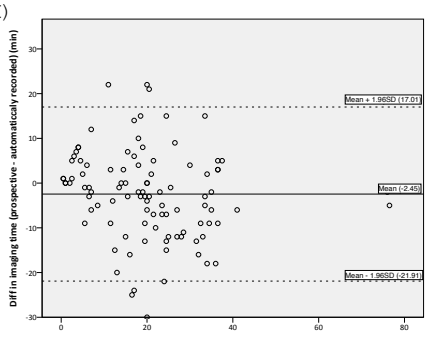
Average time to CT by two measuring methods

E)



Average TR-intervention time by two measuring methods

C)



Average total imaging time by two measuring methods

Abbreviations: SD, standard deviation; TR, trauma room; ICU, intensive care unit; Int, intervention.

Table 4 ISS versus trauma room time (dedicatedly registered) in minutes

ISS	Dedicated time registration	Routinely recorded	P-value
1-15 (n = 80)	46 (32–62)	42 (27–56)	0.001
16-24 (n = 11)	53 (40–71)	43 (37–90)	0.756
25-75 (n = 9)	44 (35–53)	38 (28–47)	0.075

Data are number (%) or median (interquartile range (IQR)). Abbreviations: ISS = injury severity score; TR = trauma room. Trauma Room time is time between arrival at and departure from the trauma room.

DISCUSSION

This study shows that routinely recorded time intervals in the trauma care setting differ statistically significant from dedicatedly registered intervals. In a convenience sample of a general trauma population, dedicated registered trauma room time is 47 minutes compared to 42 minutes routinely recorded in hospital databases. Time to start CT is longer when dedicated registered as well. Bland-Altman plots also show that there is considerable discrepancy between the two measurement methods with wide limits of agreement. It depends on the research topic whether wide intervals are acceptable.

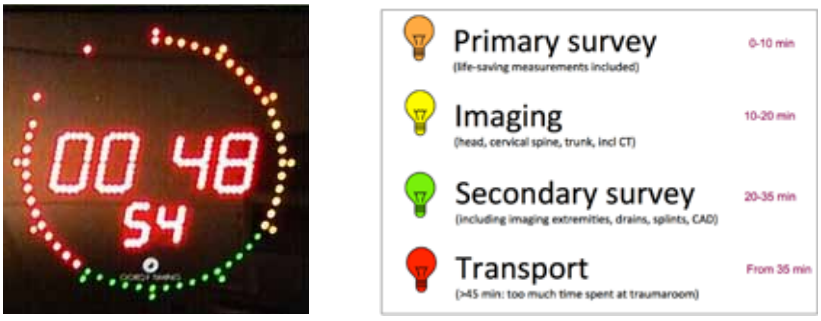
We believe that most hospitals would argue that time points registered in their hospital databases are in fact dedicatedly collected data. Although this should ideally be the case, we hypothesized that it is well possible that time points retrieved from hospital databases are less prospective and less accurate then we assume. For example, admission and departure times are registered by hand in the medical record by personnel which has other (potentially more important) duties in patient care as well. Therefore we compared those time points with purely dedicatedly collected time points. This dedicated and purely prospective form of data collection is performed in several centers in Germany as well, by using dedicated software to collect data including time intervals for the national trauma registry.[14]

Since clinically relevant time intervals in trauma care are used as quality indicators in the ACS NSQIP program, we wondered whether time points that are registered in hospital databases are reliable enough to be used as such. We did not formulate an a priori assumption about the relevant difference between recordings since this is highly dependent on the specific purpose of the measurement the recordings are used for. In case of life-saving measures differences of minutes could be relevant while greater differences could be accepted in case of other research topics.

Time intervals are useful as quality indicators when they reflect the efficiency of the provided trauma care. It should be fully clear that gaining time in trauma care should not be an aim in itself. Trauma care is suited to the unique needs of each patient and all medically indicated diagnostic and interventional procedures should be performed, regardless of the time it takes. This is reflected by our finding that patients with an ISS between 16 and 24 have the longest trauma room time: these patients are mostly hemodynamically stable enough to remain at the trauma room where central lines can be placed, tubes and drains can be inserted and most diagnostics can be realized. However, during the current economic challenging times in health care, efficient time management in the trauma room is desirable. This will make the trauma room available for new admissions and it will allow medical, nursing and other personnel involved to shift their attention (back) to other, more or less urgent patients, or other (non-clinical) duties.

To raise the awareness of time management during trauma care in our hospital, a specially developed trauma clock is attached to a wall in the trauma room (Figure 2). The colours of the LED light in the outer circle represent time intervals relevant during trauma care and correspond with the adjoining poster. The following target time points were set up: the primary survey should be finished in 10 minutes (orange), another 10 minutes are needed to do radiologic imaging (yellow), the consecutive 15 minutes are used for secondary survey (green) and preferably, after 35 minutes a patient should be ready for transport (red). Although no formal research on this topic has been done yet, we have the impression that the clock raises the awareness of time management during trauma care. Especially young residents, for whom the learning experience of being the trauma team leader is demanding itself, mention that they are more aware of the time they spend in the trauma room with each patient. The Trauma Clock is currently being further refined and made commercially available (adjustments are possible according to local specifications and wishes).

Figure 2 Trauma Clock and adjoining poster



Dedicatedly registered intervals might be preferred above routinely recorded time intervals when used as quality indicators, but this method is labour-intensive. An alternative is improving the

routinely registered time intervals. This could be done by linking routinely recorded time intervals to routinely executed actions at the trauma room. A pressure plate in the entrance of the trauma room, that automatically records time of arrival, for example. An automatically recorded time of arrival when the patient is connected to the monitoring device is an inexpensive alternative. Besides registering time intervals dedicatedly or by linking routinely recorded time intervals to routinely executed actions there is a third option. This is the use of Real-Time Location Systems like radio-frequency identification (RFID).[15] The way RFID works is simple. A small tag on a device or person emits a radio wave that is detected by a network of receivers around the hospital. Software states the position of the patient and puts the location into a hospital information system. The same software can link time intervals to the location. This creates a very accurate way of recording time intervals. Though it is expensive to build such an infrastructure, it can help the staff to work more efficiently by providing them with real-time information.

Limitations and strengths

The main limitation of our study is the size of the patient sample and the subsequent relatively small absolute amount of multi trauma patients. Differences might be greater than we assume in a larger study population, although the characteristics of the study population are representative for trauma patients in our center and included patients did not differ in baseline characteristics from excluded patients.

Another limitation is that the compared time intervals are both at least partially biased by human factors. Not all routinely recorded time intervals are therefore strictly 'routinely recorded', trauma room time and ICU time for example depend on human factors at least partially. However, our aim was to assess the reliability of time intervals as recorded in our hospital databases. These time intervals are used for research purposes and were therefore not corrected for bias in human factors. Furthermore, we could have validated the dedicated time registrations by a second independent observer or video recording. However, video recording might be even more subjective than 'on-scene' registrations, since not all actions might be visible. The independent researcher was not involved in trauma care and his only task was to register the time intervals thereby reducing the risk of bias.

Strength of our study is that it reflects daily practice. Most retrospective studies use routinely recorded time intervals under the assumption that these intervals correspond with the real intervals. To our knowledge, this is the first study on the topic of trauma patients that questions this assumption. Especially when time intervals are used as quality indicators, it is of major importance to know whether these time intervals are realistic enough to be judged on. Furthermore, we developed a device which can be useful in increasing the awareness of the passing of time during trauma work-up.

CONCLUSION

This study shows that routinely recorded time intervals in the trauma care setting differ statistically significant from dedicatedly registered intervals.

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3

SPLIT BOLUS TECHNIQUE IN POLYTRAUMA: A PROSPECTIVE STUDY ON SCAN PROTOCOLS FOR TRAUMA ANALYSIS

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ABSTRACT

Objective For the evaluation of severely injured trauma patients a variety of total-body CT scanning protocols exist. Frequently multiple pass protocols are used. A split bolus contrast protocol can reduce the number of passes through the body, and thereby radiation exposure, in this relatively young and vitally threatened population. The purpose of this study is to evaluate three protocols for single pass total-body scanning in a 64-slice MDCT on optimal image quality.

Methods Three total-body CT protocols were prospectively evaluated in three series of 10 consecutive trauma patients. In Group A unenhanced brain and cervical spine CT was followed by chest–abdomen-pelvis CT in portovenous phase after repositioning of the arms. Group B underwent brain CT followed by a one-volume contrast CT from skull base to the pubic symphysis without arm repositioning. Group C was identical to Group A, but the torso was scanned with a split bolus technique. Three radiologists independently evaluated protocol quality scores (5 point Likert scale), parenchymal and vascular enhancement and artifacts.

Results Overall image quality was good (4.10) in Group A, more than satisfactory (3.38) in Group B, and nearly excellent (4.75) in Group C ($P<0.001$). Interfering artifacts were mostly reported in Group B in the liver and spleen.

Conclusion In single pass total-body CT scanning a split bolus technique reached the highest overall image quality compared to conventional total-body CT and one volume contrast CT.

INTRODUCTION

Computed Tomography (CT) imaging in trauma has become increasingly important and prevalent.[1-8] Recently the beneficial effect of total-body CT scanning on mortality in severe trauma patients was reported when compared to selective CT scanning after conventional work up.[9] Although rapid diagnosis led to an increase in probability of survival, some criticism followed, focussing on the increased radiation exposure in this relatively young population.[10-12]

In most centers that perform a total-body CT in trauma patients, the technique comprises a multidetector CT (MDCT) of the head, cervical spine, chest and abdomen. Despite this consensus in the scanned volume, a considerable variation in the scan protocols is seen in different trauma centers around the world.[2,4-9,13,14] This variation includes contrast timing and number of phases. Of note, the term pass reflects merely the acquisition of a single scan series, whereas contrast phase points at a certain time after administration of contrast medium targeted at the specific enhancement of organs of interest. When up to four passes through the body (non-contrast, arterial, portovenous phase and excretion phase) are used, this could lead to higher and unnecessary radiation exposure. However, only a paucity on data on the quality of protocols exist[13,14], and no prospective study so far for a 64-slice CT scanner.

In this study we evaluated three different scan protocols (portovenous contrast phase, with and without arm repositioning and split bolus contrast technique) with respect to quality and scan times. The aim of this study was to evaluate three protocols for single pass total-body scanning in a 64-slice MDCT on optimal image quality.

PATIENTS AND METHODS

The present study was a single center prospective study performed at a level-1 university trauma center in The Netherlands as a pilot study before the start of a multicenter, randomized trial on total-body CT in trauma patients (April 2011). Our trauma resuscitation room has a sliding gantry 64-slice CT-scanner (Sensation 64, Siemens Medical Solutions, Forchheim, Germany) with a multifunctional, radiolucent trauma resuscitation table.[15,16] All consecutive polytrauma patients who were admitted during day time were eligible. Inclusion criteria for total-body CT scanning were: life-threatening problems (respiratory rate >29 or <10, or pulse >120/min, systolic blood pressure < 100 mmHg, exterior blood loss > 500 ml, or Glasgow Coma Score ≤ 13 or abnormal pupils), or clinical signs of flail chest, open chest, multiple rib fractures, pelvic fracture, unstable vertebral fractures, spinal cord compression or fractures of at least two long bones. Exclusion criteria were: age <18 years, known pregnancy, patients referred from other hospitals or any patient judged too unstable to undergo scanning and requiring resuscitation or immediate operation. All patients were followed during the complete hospital stay. The study was approved by the local Ethics Committee, with a waiver of informed consent.

Imaging protocol

Three different trauma scan protocols were evaluated. Inclusion took only place during office hours when at least one of the investigators was present to control the work flow and perform time registration. Three series of 10 patients were included. No randomization was performed; after every 10 consecutive inclusions the protocol was changed for the next 10 patients.

All patients received a CT of the brain, cervical spine, chest and abdomen/pelvis. Scan parameters were equal in the three groups: collimation 64 * 0.6 mm with 120 kV and 380 mAs for brain, reference mAs of 250 for cervical spine and 200 for body, rotation time 1.0 sec for brain and cervical spine and 0.5 for chest/abdomen, with standard pitch of 0.85, 0.9 and 1.4, for the respective body parts (median Dose Lenght Product (DPL) of the torso was 1125, 1125 and 1128 mGy-cm for the three respective groups). The protocols for cervical spine and torso used a 4D automatic tube current modulation (CARE dose 4D Automatic Exposure Control, Siemens, Forchheim, Germany). During scanning no gantry tilt was used. Intravenous contrast (Optiray® 350 125 ml Pre fill, Covidien Mallinckrodt, Cincinnati, OH, USA) was administered via a 18G peripheral cannula in the right antecubital vein. Preset contrast medium protocols were programmed in the injection device (Optivantage DH injector, Covidien Mallinckrodt). In all three groups administration of intravenous contrast medium was followed by a saline chase of 40 ml at 4 ml/s. Brain reconstruction was in axial planes with 5 mm head kernel and 1 mm bone kernel, cervical spine in axial, sagittal and coronal planes 1 mm bone kernel. Torso was reconstructed at 3 mm axial and coronal slices in soft and bone kernel.

The following scanning protocols were compared:

Group A. Conventional total-body trauma CT. Non-contrast enhanced CT brain and cervical spine with arms alongside the patient, after which arms were elevated and positioned alongside the head followed by CT of chest / abdomen/ pelvis after administration of 100 ml intravenous contrast medium at a rate of 4 ml/s in the venous phase, started after 60 seconds.

Group B. One volume contrast CT. Non-contrast enhanced CT of the brain, followed by a contrast enhanced volume-CT from skull base until the pubic symphysis, 4 ml/s with fixed delay of 30 seconds and arms alongside the body. Cervical spine was included into this torso scan, with the upper abdomen generally scanned in a late arterial phase.

Group C. Split Bolus. Equal to Group A, but with split bolus technique: non-contrast enhanced CT of the brain and cervical spine, followed by repositioning of the arms alongside the head and scanning the torso with a fixed delay split bolus: at 60 sec before start of the CT 80 ml intravenous contrast medium at a rate of 4 ml/s and saline chase, followed at 20 seconds before start of the CT by 40 ml contrast medium at a rate of 5 ml/s and saline chase.

Evaluation

Subjective image quality was assessed on a standardized form independently by three radiologists with 6, 8 and 12 years of experience in trauma imaging. These observers were blinded for patient data and scanning protocols. All studies were evaluated using a picture archiving and communication system PACS (Impax 4.5, AGFA Gevaert, Mortsel, Belgium). Qualitative image assessment focused primarily on organ/vessel delineation in combination with its homogeneity of enhancement. A lower score was attributed when artifacts significantly hindered this evaluation. Subjective scores for image quality were recorded for the overall quality of the total-body CT scan and on specific body regions: brain, cervical spine, thoracolumbar spine, lung parenchyma, mediastinum, liver, spleen, kidney, pelvis, and aortic arch, abdominal aorta at level of the superior mesenteric artery, and portal vein. For this assessment a 5 point Likert scale was used: 1- non diagnostic image quality; 2- poor image quality; 3- satisfactory; 4- good image quality and 5- excellent image quality. Hounsfield Units (HU) attenuation determined by setting a region of interest (ROI) half of the vessel caliber for the aortic arch, abdominal aorta and the portal vein were registered, as well as in the parenchyma of the liver, spleen and renal cortex using a 1 cm ROI. In case artifacts were present, the type of artifact, location and interference with evaluation were noted.

Several time points were registered: time of admission, start and end of CT acquisition (scout view and last axial image respectively), time of diagnosis for treatment planning and time of departure from the trauma resuscitation room.

Statistical analysis

Differences between patient series were assessed by Fisher's exact test (gender) and one-way analysis of variance (age and injury severity score (ISS)). Differences between the three investigated protocols in image quality scores were assessed by balanced univariate analyses of covariance with adjustment for differences among radiologists. Differences between protocols by contrast enhancement values and acquisition times were assessed by balanced univariate analysis of variance. A value of $P < 0.05$ was considered statistically significant. Bonferroni correction was applied during post hoc comparisons.

The intra-class correlation coefficient (ICC) was used to measure inter-observer absolute agreement among the three reviewers on image quality. The ICC values with a 95% confidence interval (95% CI) were calculated using a two-way mixed-effects model with single measures. The ICC is an index of concordance that indicates the degree of agreement beyond that expected by chance alone, and is appropriate when assessing agreement between two or more observers. ICC values higher than 0.8 were considered to represent almost perfect concordance, values between 0.61 and 0.8 as substantial, between 0.41 and 0.6 as moderate, between 0.21 and 0.4 as fair, between 0.0 and 0.2 as slight, and below 0.0 as poor according to the Landis

and Koch classification.[17] Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS version 18.0, SPSS Inc. Chicago, IL, USA).

RESULTS

Thirty consecutive patients were included, of which the demographics are displayed in Table 1. The three groups differed by age, with older patients in Group C and younger patients in Group B.

Table 1 Demographics for conventional (Group A), one volume contrast (Group B) and split bolus protocol (Group C) total body trauma CT

	Group A n=10	Group B n=10	Group C n=10	P-value
Age (mean, SD)	52.6 (23.2)	41.3 (21.0)	60.5 (21.1)	<0.001
M:F	6/4	8/2	8/2	0.67
Mechanism of injury				1.00
Blunt	9	10	10	
Sharp	1	0	0	
ISS (mean, SD)	17.3 (15.4)	28.7 (20.9)	32.2 (20.9)	0.21
Mortality (cause of death)	2 (TBI, stroke)	2 (TBI)	4 (TBI n=2, SCI, pulmonary edema)	

Abbreviations: M, male; F, female; ISS, injury severity score; TBI, Traumatic Brain Injury; SCI, Spinal Cord Injury

Figure 1 Axial and coronal reformatted images (3 mm soft kernel) of 3 trauma patients of Group A (conventional total-body trauma CT with CT scanning of the body in venous phase after repositioning of the arms), Group B (one volume contrast enhanced CT from skull base until the pubic symphysis) and Group C (split bolus technique).

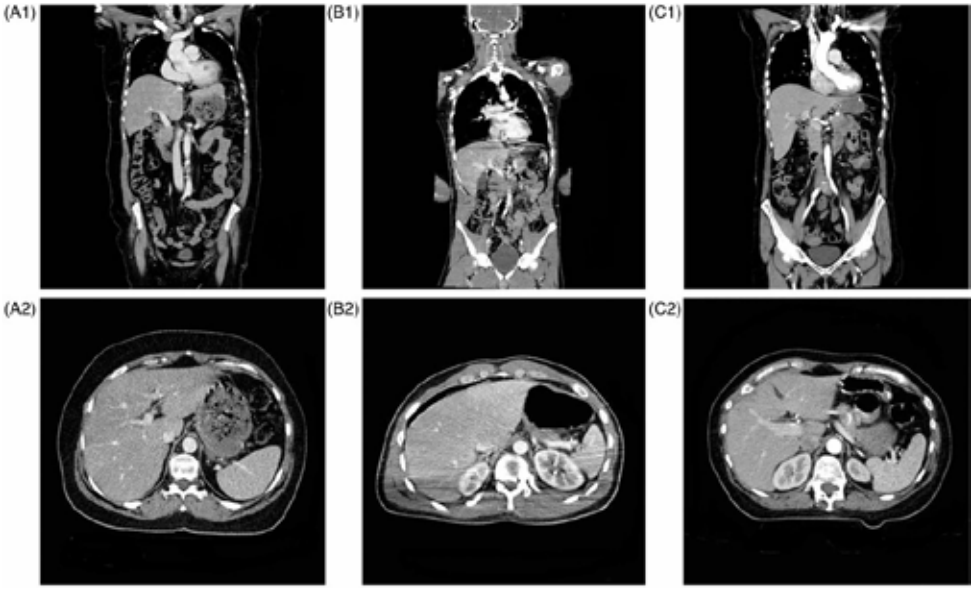

Table 2 shows that overall quality was rated nearly excellent (4.75) in the split bolus Group C, good (4.1) in the conventional Group A, and more than satisfactory in the one volume Group B (3.38), all differences being significant. For parenchymal evaluation of the liver and spleen Group B was of significantly lesser quality ($P<0.001$) compared to Group A and C. Image quality of the kidney and pelvis were higher in Group C compared to Group B ($P=0.002$ and $P=0.031$, respectively). Image quality of the abdominal aorta was higher in Group C than in the other two groups ($P=0.014$) and of the portal vein higher than in Group B ($P=0.01$). No quality differences were recorded for brain, cervical and thoracolumbar spine, lung, and mediastinum between the three groups.

Table 2 Quality evaluation and main vessel enhancement in total-body CT using conventional (Group A), one volume contrast (Group B) and split bolus protocol (Group C)

	Group A n=30	Group B n=30	Group C n=30	F-test; P
Quality				
Overall	4.10 (0.76)	3.38 (0.87)	4.75 (0.43)	27.6; <0.001
Brain	3.40 (0.67)	3.50 (0.51)	3.23 (0.73)	2.5; 0.09
C-spine	3.83 (0.84)	3.97 (0.77)	3.93 (0.83)	0.3; 0.73
Lung	4.10 (0.80)	3.87 (0.94)	4.10 (0.80)	0.9; 0.40
Aortic arch	3.27 (1.08)	3.83 (1.02)	4.17 (0.99)	6.5; 0.002
Mediastinum	4.00 (0.79)	4.03 (0.67)	4.17 (0.65)	0.9; 0.39
TL-spine	4.27 (0.64)	4.10 (0.66)	4.33 (0.61)	1.3; 0.27
Abdominal aorta	3.77 (0.93)	3.83 (0.91)	4.47 (0.86)	7.3; 0.001
Portal vein	3.70 (1.09)	3.13 (1.36)	3.93 (0.91)	4.9; 0.01
Liver	3.80 (1.13)	2.83 (0.99)	3.93 (0.94)	14.1; <0.001
Spleen	3.77 (1.13)	2.93 (1.08)	4.10 (0.80)	13.7; <0.001
Kidney	3.90 (0.96)	3.63 (0.85)	4.30 (0.53)	6.2; 0.003
Pelvis	4.13 (0.86)	4.00 (0.79)	4.43 (0.57)	3.6; 0.031
Enhancement (HU)				
Aortic arch	177.8 (86.7)	226.1 (54.2)	275.9 (74.4)	13.3; <0.001
Abdominal aorta	172.8 (88.7)	174.9 (43.2)	241.4 (81.4)	8.2; 0.001
Portal vein	140.3 (55.2)	155.6 (34.9)	155.5 (33.2)	1.3; 0.28
Liver	82.9 (30.1)	89.2 (17.8)	78.0 (18.8)	1.8; 0.17
Spleen	103.6 (26.8)	118.4 (24.3)	120.4 (24.8)	3.8; 0.025
Kidney	165.1 (46.1)	170.4 (40.5)	177.2 (40.4)	0.6; 0.54

Data are expressed as mean (standard deviation). Abbreviations: C-spine, cervical spine; TL-spine, thoracolumbar spine; HU, Hounsfield Unit. A 5 point Likert scale was used ranging between 1- non diagnostic image quality, and 5 –excellent image quality. *Three radiologists each assessed the same 10 patients per protocol.

Contrast enhancement values for the aortic arch were highest in Group C, followed by Group B and Group A. HU-values in the spleen (P=0.039) and abdominal aorta (P=0.002) were lower in Group A compared to Group C. Lower HU-values compared to Group C were observed for Group B in the abdominal aorta (P=0.003). Otherwise, no significant differences in contrast enhancement values were observed.

In one patient in group A and one patient in group B breathing artifacts were reported. In one patient in group A evaluation of the neck was disturbed by a necklace. Interfering beam hardening artifacts were noted in three patients in the upper abdomen in Group B, more precisely the liver and spleen, due to the proximity of the arms.

Table 3 Time intervals for total-body CT scanning using conventional (Group A), one volume contrast (Group B) and split bolus scan protocol (Group C)

Interval	Group A	Group B	Group C	F-test; P
Total CT scanning time	8.7 (2.4)	4.8 (1.4)	6.7 (1.6)	10.9; <0.001
CT to diagnosis time	9.8 (3.6)	11.0 (3.7)	11.6 (3.8)	0.6; 0.55
Admission to diagnosis	29.5 (6.2)	27.0 (3.0)	32.7 (10.3)	1.6; 0.22
Total trauma room time	40.0 (6.1)	45.2 (13.6)	37.2 (16.6)	1.0; 0.40

Data are expressed in minutes as mean (standard deviation) unless otherwise indicated. F-test by two-way ANOVA. Abbreviations: CT, Computed Tomography.

The scanning protocol used in Group B was significantly shorter (4.8 minutes) than in Group A (8.7 minutes; P<0.001). There was no significant difference between the duration of the scanning protocol in Group B compared to Group C (6.7 minutes; P=0.092) (Table 3). Time from acquisition of CT to diagnosis was similar for the three groups.

Table 4 Inter-observer absolute agreement among the three observers on image quality in total-body CT using conventional (Group A), one volume contrast (Group B) and split bolus protocol (Group C).

	Group A n=10	Group B n=10	Group C n=10
Radiologists (n)	3	3	3
Overall	0.61 (0.24, 0.87)	0.17 (-0.12, 0.60)	0.28 (-0.06, 0.68)
Brain	0.30 (-0.01, 0.69)	0.00 (-0.07, 0.20)	0.11 (-0.04, 0.43)
C-spine	0.28 (-0.02, 0.67)	0.15 (-0.19, 0.61)	0.10 (-0.03, 0.41)
Lung	0.00 (-0.12, 0.31)	0.21 (-0.11, 0.63)	0.37 (0.03, 0.75)
Aortic arch	0.60 (0.24, 0.86)	0.11 (-0.12, 0.51)	0.46 (0.10, 0.8)
Mediastinum	-0.01 (-0.11, 0.26)	0.02 (-0.09, 0.31)	0.09 (-0.06, 0.42)
TL-spine	0.12 (-0.10, 0.52)	0.13 (-0.16, 0.57)	0.03 (-0.15, 0.41)
Abdominal aorta	0.55 (0.15, 0.85)	0.31 (0.00, 0.70)	0.44 (0.08, 0.79)
Portal vein	0.42 (0.06, 0.77)	0.05 (-0.17, 0.46)	0.12 (-0.08, 0.50)
Liver	0.30 (-0.01, 0.69)	0.37 (0.00, 0.75)	0.09 (-0.03, 0.38)
Spleen	0.29 (-0.01, 0.68)	0.60 (0.24, 0.86)	0.04 (-0.05, 0.27)
Kidney	0.22 (-0.08, 0.64)	0.38 (0.01, 0.75)	0.00 (-0.07, 0.21)
Pelvis	0.02 (-0.17, 0.41)	0.2 (-0.05, 0.59)	-0.06 (-0.18, 0.25)

Data are expressed as intraclass correlations coefficients (95% confidence interval).
Abbreviations: C-spine, cervical spine; TL-spine, thoracolumbar spine.

The inter-observer absolute agreement among the three reviewers on overall image quality was substantial for the conventional protocol Group A, slight for the one volume Group B, and fair for the split bolus Group C (Table 4). For head and neck it ranged between slight and fair, and for chest agreement ranged between poor and moderate with the highest value (0.6) for the aortic arch in Group A. For the abdomen agreement also varied between poor and moderate with the highest agreement (0.6) achieved for Group B on the spleen.

DISCUSSION

This study shows that the split bolus technique for single pass total-body CT scanning had the highest overall image quality, compared to the conventional total-body trauma CT and the one volume contrast CT protocol. A split bolus technique combines different contrast phases into one acquisition, thereby diminishing radiation exposure with only limited increase of the amount of contrast medium. It is most frequently used in renal imaging.[18,19] In trauma only three reports on a multi-phasic scan protocol in MDCT have been published.[20-22] Loupatatzis et al. compared in 16-slice MDCT a tri-phasic injection scheme (70 ml at 3 ml/s, followed by 0.1 ml/s for 8 seconds, and 70 ml at 4 ml/s) to their standard CT angiography protocol.[20] The tri-phasic protocol achieved similarly high image quality for arteries compared to standard CT angiography protocol, parenchymatous organs had better image quality compared to specialized protocols. As in our study arm, artifacts reduced the enhancement of spleen and liver parenchyma. In a retrospective study, Yaniv and colleagues compared the same contrast protocol set up for 64-slice MDCT with an arterial-phase contrast-enhanced CT of the thorax and a portovenous scan of the abdomen and pelvis, but added a preceding unenhanced CT of the abdomen.[21] The tri-phasic injection protocol enabled better vascular and abdominal parenchymal imaging, although mean enhancement values in the aorta were significantly greater with the conventional protocol. Nguyen et al. compared a standard injection protocol with an one-volume acquisition from the circle of Willis to the pubic symphysis in 16-slice MDCT using a biphasic (150 ml, at 6 and 4 ml/s) or mono-phasic (110 ml at 4 ml/s, 400 mg I/ml) injection.[22] No significant differences were found in mean enhancement values in the aorta, liver, spleen, and kidney for the three protocols. Quality scores were significantly higher for liver, spleen and kidney with the arms above the head compared to arms alongside the body. Single-pass protocols had significantly shorter median acquisition times than the conventional protocol. Hence, our findings for 64-slice MDCT are in concordance with these previous CT studies.

In blunt abdominal trauma an arterial phase is more sensitive for the detection of intrasplenic pseudoaneurysms, but a portal venous phase is more sensitive for the detection of parenchymal injuries and active bleeding of the spleen.[23] Dual phase CT can be considered as a complete work up as it has better overall diagnostic performance than single phase CT. However, this is at the cost of doubling radiation exposure to the abdomen. As group B is scanned in a late arterial phase, it could be inferior in case of active bleeding and parenchymal injuries. Whether the theoretical superposition of an arterial on a portal venous phase in split bolus provides a comparable complete performance as dual phase imaging has to be proven in a large prospective study.

Total-body CT can also be useful to diagnose blunt cerebrovascular injuries.[24-26] Only protocol B offered the possibility to screen for these injuries. The split bolus protocol can theoretically

also fulfill these requirements, though was not investigated in our study. It was, however, satisfactorily used in later patients if during CT acquisition a skull base or upper cervical spine fracture was seen. Although injuries of the supra-aortic vessels are rare after blunt trauma, these cerebrovascular injuries are associated with fractures of the cervical spine or skull base.[27]

Time is essential in trauma, as underlined by the ATLS® philosophy "time is life". We observed a time difference between the protocol without repositioning of the arms and the other two protocols with arm repositioning. Remarkably, only few reports have focussed on this important work flow aspect in correlation with scan protocols.[14,28-30] Whether the slight time gain can outweigh the observed lower diagnostic quality remains to be seen.

We did not focus on radiation exposure in our study. However, Brink et al. found that scanning with the arms alongside the body resulted in a 45% increase in radiation exposure and a decrease in image quality compared to scanning patients with a cranial position of the arms.[31] Recently this has been confirmed by two other studies.[32, 33]

Limitations

Our study has several limitations. First, there are different combinations and settings possible when considering contrast medium phases (non-enhanced, arterial, venous, delayed phases) and body regions (head, neck, thorax, abdomen/pelvis and extremities). We only studied three different contrast protocols, and therefore we cannot make a statement on other variations. Secondly, patients' BMI or weight was not known. Since contrast enhancement of the liver parenchyma is influenced by body weight, differences in liver enhancement and subsequently in quality of liver imaging may be caused by differences in body weight between patients. For the split bolus group ROI triggering in the thoracic aorta probably could have resulted in higher arterial enhancement values. On the other hand, targeted planning by the technician would have resulted in a more complicated procedure and longer examination times. Fixed delay appears to be more practical in this stressful circumstance and therefore less error-prone. Further, diagnosis time, admission to diagnosis time, and total room time are not only influenced by the type of CT scan protocol but also by the specific types of injuries and by emergency room management factors. Total-body CT scanning time is therefore the most relevant time factor comparing group A, B and C. A final limitation concerns the restricted sample size for the assessments of differences among the imaging protocols. After checking whether the data fulfilled the test conditions, it was noted that homogeneity of variances could not be assumed (i) for the contrast enhancement values for portal vein and liver, and (ii) the acquisition time between admission and diagnosis. The corresponding P-values of the ANOVA tests are well above 0.05, but should nevertheless be interpreted with some caution. Although unlikely, these results may be false negative. Of note, in our series no important missed diagnosis during follow up was recorded. Since the end of the study we used the split bolus technique in all following cases as part of an

international multicenter randomized trial on total-body CT in severe trauma patients.[34] Further experience requiring more prospective studies are needed to evaluate its clinical accuracy.

CONCLUSION

In conclusion, evaluation of three scanning protocols for single pass total-body CT in severe trauma patients showed that the split bolus technique reached the highest scores in image quality and vascular and parenchymal enhancement. The one volume contrast CT protocol was quickest and can probably be used in selected cases where time gain of some minutes could potentially outweigh the reduced image quality.

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4

A CASE-MATCHED SERIES OF IMMEDIATE TOTAL-BODY CT SCANNING VERSUS THE STANDARD RADIOLOGICAL WORK-UP IN TRAUMA PATIENTS

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ABSTRACT

Objective In recent years Computed Tomography (CT) has become faster and more available in the acute trauma care setting. The aim of the present study was to compare injured patients who underwent immediate total-body CT scanning with patients who underwent the standard radiological work-up with respect to 30-day mortality.

Methods Between January 2009 and April 2011, 152 consecutive patients underwent immediate total-body CT scanning as part of a prospective pilot study. These patients were case-matched by age, gender and Injury Severity Score category with control patients from a historical cohort (July 2006 – November 2007) who underwent X-rays and FAST followed by selective CT scanning.

Results Despite comparable demographics, TBCT patients had a lower median Glasgow Coma Score than controls (10 vs. 15, P<0.001) and on-scene endotracheal intubation was performed more often (33% vs. 19%, P=0.004). Thirty day mortality was 13% in the TBCT patient group vs. 13% in the control group (P=1.000). A generalized linear mixed model analysis showed that a higher in-hospital Glasgow Coma Score (Odds Ratio (OR) 0.8, 95% confidence interval (CI) 0.745-0.86; P<0.001) and immediate total body CT scanning (OR 0.46, 95%CI 0.236-0.895; P=0.022) were associated with decreased 30-day mortality, while a higher Injury Severity Score (OR 1.054, 95%CI 1.028-1.08; P<0.001) was associated with increased 30-day mortality.

Conclusion Trauma patients who underwent immediate total body CT scanning had similar absolute 30-day mortality rates compared to patients who underwent conventional imaging and selective CT scanning. However, immediate TBCT scanning was associated with a decreased 30-day mortality after correction for the impact of differences in raw ISS and in-hospital GCS.

INTRODUCTION

Traumatic injuries are an important cause of death among people 15-60 years of age, and the effects on the lives of those who survive may be devastating.[1,2] Safe, accurate and rapid diagnostic procedures make sure that treatment can be planned and carried out as soon as possible. If we can speed up the diagnostic work-up in injured patients, this may help to prevent deaths.

In recent years Computed Tomography (CT) has become faster, more detailed and more available in the acute trauma care setting.[3-5] Hence, the standard radiological work-up (X-rays and Focussed Assessment with Sonography for Trauma (FAST) followed by selective CT scanning) may no longer be the optimal choice of primary diagnostics. One area in particular that has gained interest in trauma care is an immediate total-body CT scan without previous conventional imaging.[3, 6-8]

Previous cohort studies have shown that immediate total-body CT scanning provides faster diagnosis in injured patients than the standard radiological workup.[9-13] In the largest retrospective study performed on this topic, patients who underwent immediate total-body CT-scanning were found to have an increased probability of survival compared to patients who underwent the standard radiological work-up.[10] This survival benefit is, however, not confirmed in absolute mortality numbers in other studies.[11, 13, 14] Wurmb and colleagues[11, 14] depicted their triage scheme but all other studies collected data of patients with an Injury Severity Score (ISS) of at least 16 who underwent a total-body CT scan. For daily practice it is of major importance to know what the selection criteria were for a patient to undergo a total-body CT and to make sure that those patients are comparable to patients who underwent the standard work-up.

The aim of the present study was to compare severely injured patients who underwent immediate total-body CT scanning according to predefined criteria with matched controls who underwent the standard radiological work-up with respect to thirty-day mortality.

PATIENTS AND METHODS

Immediate Total-Body CT scanning: TBCT patients

Between January 2009 and April 2011 patients in whom severe injury was suspected, based on predefined vital signs and clinically suspicious diagnoses, underwent immediate total-body CT scanning as a pilot study for the REACT-2 trial.[15] In- and exclusion criteria for this pilot study are given in Table 1.

This study was approved by the Institutional Review Board with a waiver of informed consent for including 50 patients. After the inclusion of 50 patients, total-body CT scanning in patients fulfilling the inclusion criteria became routine in our level-1 trauma center. All consecutive injured patients who received total-body CT scanning in this period according to the criteria defined in Table 1 were therefore included in this study and will be described as 'TBCT patients'.

During the primary survey the vital functions were checked and, when necessary, corrected. The necessary corrections and interventions during the primary survey consisted of intubation or performing a cricothyrotomy, chest tube drainage or pericardiocenthesis and taking hemorrhage-controlling measurements such as applying a pelvic binder or external pressure. Furthermore, at least one working infusion system should be available and blood could be drawn for analysis before making the CT scan.

Total-body CT scanning consisted of a two-step whole-body acquisition (from vertex to pubic symphysis) starting with Head and Neck Non Enhanced CT (NECT) with arms alongside the body. For the second complementary scan a split-bolus intravenous contrast protocol was used directly after repositioning the arms alongside the head. This scan covered chest, abdomen and pelvis.

Standard radiological work-up: control patients

Patients admitted between July 2006 and November 2007 underwent the standard radiologic work-up. During this period, the REACT-1 trial[16] was recruiting all blunt trauma patients who were admitted to our hospital. Standard radiological work-up consisted of chest X-ray, pelvic X-ray and FAST followed by selective CT scanning based on local imaging guidelines.

Conventional digital radiographs were made by a mobile X-ray machine and archived in the Picture Archiving and Communication System PACS (Impax 4.5, AGFA Gevaert, Mortsel, Belgium). Portable ultrasound was available to perform FAST. The trauma resuscitation room was further equipped with a sliding gantry CT-scanner (since 2008 a 64-slice CT scanner, before that period a 4-slice CT scanner was used) (Sensation 64, Siemens Medical Solutions, Forchheim, Germany) with a multifunctional, radiolucent trauma resuscitation table.

Table 1 Criteria for immediate total-body CT-scanning in TBCT patients

Trauma patients with the presence of one of the following vital parameters:
o respiratory rate >29/min or <10/min;
o pulse >120/min;
o systolic blood pressure < 100 mmHg;
o estimated exterior blood loss > 500 ml;
o Glasgow Coma Score ≤ 13;
o abnormal pupillary reaction on site.
OR patients with one of the following clinically suspicious diagnoses:
o fractures from at least two long bones;
o flail chest, open chest or multiple rib fractures;
o pelvic fracture;
o unstable vertebral fractures;
o spinal cord compression.
Trauma patients not receiving total-body CT scanning:
o known age <18 years;
o known pregnancy;
o referred from another hospital;
o any patient who is judged to be too unstable to undergo a CT scan and requires (cardiopulmonary) resuscitation or immediate operation.

Data collection and processing

Data concerning patient demographics, radiologic imaging, type of treatment and clinical outcome were prospectively registered in a database by a dedicated research nurse for the control patients and by a trained medical student under supervision of a physician for the TBCT patients. Pre-hospital parameters (hypotension defined as systolic blood pressure below 90 mmHg, on-scene Glasgow Coma Score and presence of endotracheal intubation) were registered as well. On-scene pre-hospital GCS was registered by the ambulance personnel. In case of on-scene intubation, in-hospital GCS was scored as 3.

Injury severity of every trauma patient was scored by trained trauma surgeons using the Abbreviated Injury Scale (AIS) per body region. Severity scores (1 to 6) within the AIS range from minor (code 1), moderate, serious, severe, critical to unsurvivable injury (code 6). AIS body regions head, chest, abdomen and extremities were described.

General practitioners and discharge locations were contacted for information concerning follow-up and hospital- and ICU days in case the patient was discharged to another hospital. In case of a deceased patient, predominant cause of death was abstracted from patient charts, computerized hospital databases and/or from information of general practitioners.

Outcome measure

Thirty-day mortality.

Matching

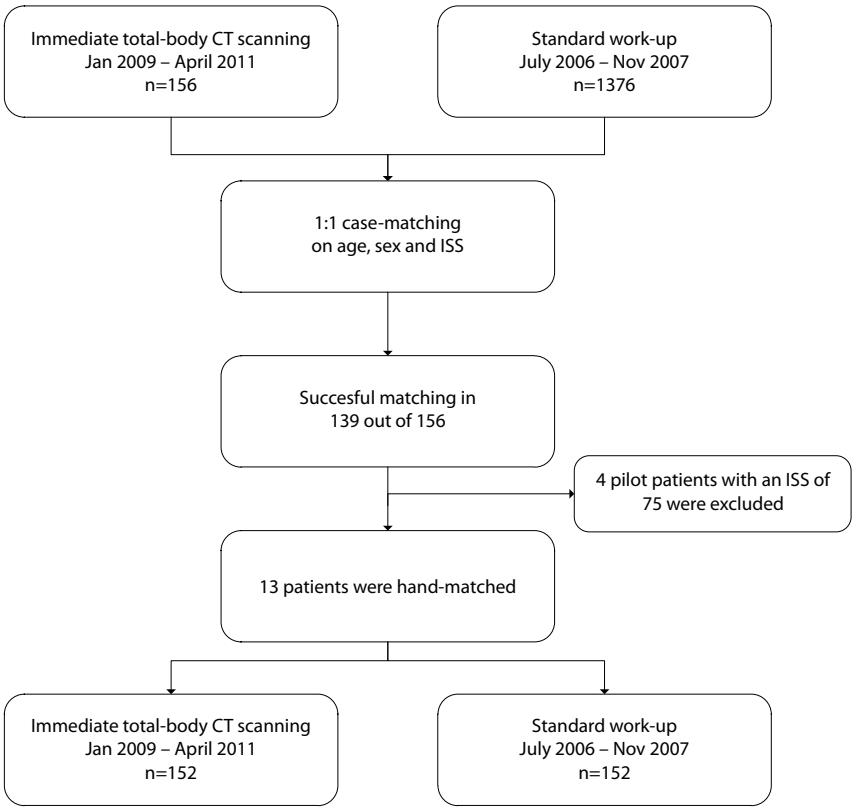
Each TBCT patient was matched 1:1 to a control patient with SPSS-syntax (from David Marso; SPSSX-L archives http://listserv.uga.edu/cgi-bin/wa?A2=ind1103&L=spssx-l&D=0&P=64620; March 30th, 2011), adapted for the following matching variables. Patients were matched by age within 5 years, gender and Injury Severity Score (ISS) category (according to the American College of Surgeons' categories of ISS: 1-9, 10-15, 16-24, >24). Matching by ISS category rather than matching by raw ISS allowed for small measurement bias to occur that resulted from the different CT scanning protocols applied, with immediate total body CT scanning tending towards slightly higher ISS values.[17]

With this method, 139 patients of 156 could be matched. Four of the 17 non-matched patients had an ISS of 75. Three died shortly after admission and one unexpectedly survived a C3-fracture with a traumatic disc hernia. Hand-matching these patients with control patients who were non-comparable in age and sex would potentially have caused selection bias. These patients were therefore excluded.

Thirteen of the non-matched patients were hand-matched by age and ISS. Age was comparable in these patients with a mean difference of 7.6 years and a maximum difference of 23 years (between females of 84 and 61 years of age). ISS was similar in these patients with a maximum difference of 2 points except in 1 patient in which the difference was 12 points (ISS of 50 and 38 in males of 93 and 80 years of age respectively). In total 152 TBCT patients were matched with 152 control patients.

The study flowchart is depicted in Figure 1.

Figure 1 Study flow chart



Standard work-up: chest and pelvic X-ray, FAST, and selective CT. Abbreviations: CT, Computed Tomography; ISS, Injury Severity Score.

Statistical analysis

Data are presented as median and interquartile ranges for not normally distributed data and as mean ± standard deviation for normally distributed data. Considering the matching of TBCT with control patients, testing was done with the McNemar test for dichotomous variables, the McNemar-Bowker test or extended McNemar test for categorical variables and with the Wilcoxon signed ranks test for continuously but not normally distributed variables.

The Revised Trauma Score (RTS) was calculated following the formula described by Champion et al.[18,19] The Trauma and Injury Severity Score (TRISS) method was used to calculate the probability of survival. [20]

Generalized linear mixed modelling was done to identify the independent predictive value of type of CT scanning for 30-day mortality, accounting for (1) TBCT patients being matched

with control patients, (2) potential confounders, and (3) multicollinearity in the predictor set. A backward stepwise approach was applied excluding predictors with the highest non-significant P-value one-by-one. A P-value below 0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS (version 20.0.0.1; IBM Coorperation) and PEPI (version 1.11; Abramson/Gahlinger, Salt Lake City, USA, 2000-2004).

RESULTS

Patient characteristics are summarized in Table 2. TBCT patients were comparable to controls with respect to mechanism of injury and laboratory results. Pre- and inhospital median Glasgow Coma Scores (GCS) were lower, while on-scene endotracheal intubation too was performed more often in TBCT patients than in controls.

Table 2 Characteristics of injured patients in the matched cohorts.

	TBCT* n=152	Controls† n=152	Missing‡	P-value
Age in years §	43.91 (19.67)	43.63 (18.61)	0	0.324‖
Men	107 (70.4%)	109 (71.7%)	0	0.687‖
Blunt trauma	147 (96.7%)	144 (94.7%)	0	0.581
Prehospital				
hypotension(SBP<90 mmHg)	4 (7.8%)	1 (2.0%)	101	0.375
intubation	48 (32.9%)	28 (19.2%)	6	0.004
GCS	12 (4-15)	15 (9-15)	17	<0.001
Trauma room				
hypotension(SBP<90 mmHg)	5 (3.4%)	7 (4.7%)	3	0.774
GCS	10 (3-15)	15 (7.3-15)	26	<0.001
Laboratory results on admission				
Hemoglobin in g/dl §	12.50 (2.00)	12.52 (1.91)	3	0.911
Ph	7.36 (7.31-7.39)	7.37 (7.31-7.42)	6	0.471
base excess in mmol/L§	-2.81 (4.34)	-3.33 (4.97)	6	0.326
ISS (points)	18 (9-29)	18 (8-29)	0	0.528
ISS in matching categories			0	1.000‖
0-9	49 (32.2%)	49 (32.2%)		
10-15	7 (4.6%)	7 (4.6%)		
16-24	34 (22.4%)	34 (22.4%)		
≥ 25	62 (40.8%)	62 (40.8%)		

Data are number (%) or median (interquartile range (IQR)) unless otherwise indicated. Abbreviations: CT, Computed Tomography; SBP, systolic blood pressure; GCS, Glasgow Coma Score; AIS, Abbreviated Injury Score; ISS, Injury Severity Score.

*Immediate total-body CT from head to pelvis. †Chest and pelvic X-ray, FAST and selective CT

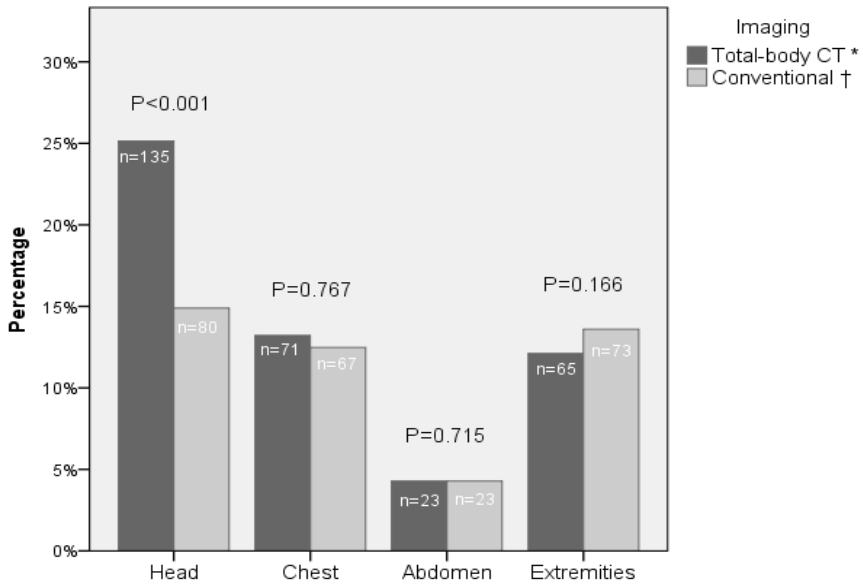
‡Missing pairs, if no data were available for at least one patient in the matched pair.

§Mean (SD). ‖Matching parameters.

Of the 152 patients in the control group, 132 patients (87%) underwent selective CT scanning of one or more body regions after conventional imaging. Twenty-two control patients (14%) underwent TBCT scanning after imaging with X-rays and FAST. Cranial CT scans were obtained in 73 patients (48%), cervical spine CT scans in 92 patients (61%), thoracic CT scans in 13 patients (9%), abdominal CT scans in 18 patients (12%), pelvic CT scans in 3 patients (2%) and thoracic or lumbar spine CT scans in 29 patients (19%).

Figure 2 shows the prevalence of severe injuries (AIS ≥3) per body region in both study groups. The TBCT patients had serious head injuries more often than the control patients did (63% vs. 37%, P<0.001). The prevalence of severe injuries to the chest, abdomen and extremities was comparable between TBCT and control patients.

Figure 2 Presence of severe injuries (AIS≥3) in the matched cohorts



* Immediate total-body CT from head to pelvis. † Chest and pelvic X-ray, FAST and selective CT.

Main results

Outcome parameters are listed in Table 3. The crude thirty-day mortality rates were 13% for both TBCT and control patients (P=1.000). Cause of death differed significantly between TBCT patients and controls (P=0.002). Five control patients who died from hemorrhage were hemodynamically unstable on admission and died at the operating room due to uncontrolled traumatic bleeding; 2 patients had no cardiac output on admission. The last patient was a drowning victim who underwent cardiopulmonary resuscitation on-scene. He was admitted to the hospital with a marked decrease in hemoglobin level with a radiologically occult bleeding

site other than subcutaneously. Other causes of death in TBCT patients were hypoxia after drowning (n=1), hypoxia after a suicide attempt by hanging (n=1), septic shock (n=1) and unexpected asystole most likely due to fat embolism (n=1). In control patients, other causes of death were out-of-hospital cardiac arrest after drowning (n=1), traumatic spinal cord lesion with complete paraplegia (n=1), fall from height while recovering from a cerebral contusion (n=1), respiratory insufficiency in combination with marginal neurologic function (n=1) and traumatic hemorrhagic complications due to anticoagulant treatment (n=1).

Type of treatment did not differ between TBCT en control patients (P=0.422). Median hospital stay was 9 days in TBCT as well as control patients (9 (IQR=3-25) vs. 9 (IQR=1-23), P=0.358).

Table 3 Outcome parameters of injured patients in the matched cohorts.

	TBCT* n=152	**Control†** n=152	**Missing‡**	**P-value**
Treatment			2	0.422
no intervention	71 (47.3%)	75 (50.0%)		
operative	74 (49.3%)	67 (44.7%)		
interventional radiology	5 (3.3%)	8 (5.3%)		
Hospital stay (days)				
overall	9 (3-25)	8.5 (1-22.8)	0	0.358
ICU stay	2 (0-6)	1 (0-5)	0	0.022
ventilation time	1 (0-3)	0 (0-1.3)	10	0.134
Discharge location			0	0.605
home	76 (50.0%)	88 (57.9%)		
other hospital	22 (14.5%)	18 (11.8%)		
rehabilitation center	14 (9.2%)	17 (11.2%)		
nursing home	11 (7.2%)	9 (5.9%)		
other	29 (19.1%)	20 (13.2%)		
Mortality			0	
24h	11 (7.25)	10 (6.6%)		1.000
30-day	20 (13.2%)	20 (13.2%)		1.000
Predominant cause of death			0	0.002
no death	128 (84.2%)	129 (84.9%)		
TBI	17 (11.2%)	8 (5.3%)		
haemorrhage	0 (0%)	8 (5.3%)		
other	7 (4.6%)	7 (4.6%)		

Data are number (%) or median (interquartile range (IQR)) unless otherwise indicated. Abbreviations: CT, Computed Tomography; SBP, systolic blood pressure; GCS, Glasgow Coma Score.

*Immediate total-body CT from head to pelvis.

†Chest and pelvic X-ray, FAST and selective CT.

‡Missing pairs, if no data were available for at least one patient in the matched pair

A generalized linear mixed model analysis was applied to assess the predictive value of type of CT scanning for 30-day mortality. Pre-hospital intubation, pre-hospital and in-hospital GCS, and raw ISS were identified as potential confounders (see Table 2). With pre-hospital and in-hospital GCS being highly correlated (Spearman's rho: 0.87), only in-hospital GCS was included in the multivariable model. Further, pre-hospital intubation was associated with higher ISS values and was dropped during the backward stepwise approach. Table 4 shows the final model, indicating that immediate total body CT scanning was associated with a lower 30-day mortality (OR 0.46, 95%CI 0.236-0.895; P=0.022) after correction for the impact of differences in raw ISS (OR 1.054, 95%CI 1.028-1.08) P<0.001) and in-hospital GCS (OR 0.8, 95%CI 0.745-0.86; P<0.001).

Table 4 Independent predictors of 30-day mortality (N=278) with GLMM

	Odds ratio	95% CI	P-value
Total-body CT scanning	0.46	0.236-0.895	0.022
Trauma room GCS	0.80	0.745-0.860	<0.001
ISS	1.054	1.028-1.080	<0.001

Abbreviations: GLMM, generalized linear mixed model; CI, Confidence Interval; CT, Computed Tomography; GCS, Glasgow Coma Score; ISS, Injury Severity Score.

DISCUSSION

This case-matched series shows that patients who underwent immediate total-body CT scanning had similar absolute 30-day mortality rates as patients who underwent conventional imaging and selective CT scanning. Patients were comparable in important prognostic factors for mortality such as age and ISS category. To correct for any non-comparable pre-hospital characteristics, a generalized linear mixed model was used, and this analysis showed that immediate TBCT was associated with decreased 30-day mortality.

The advantages of TBCT scanning in the clinical setting seem clear: TBCT scanning saves time. A rapid overview of all threatened body regions can be obtained in 15 minutes, which leads to rapid decision making in treatment. As a result of goal-directed and earlier start of treatment, mortality could be reduced. Previous studies were too focussed on TBCT scanning and mortality in injured patients, but whether this scan was 'immediate', as was the case in the present study, that fact was not described routinely. Differences in overall, 24h of 30-day mortality in favor of immediate TBCT have been described previously[8,10,21,22], but there is no reproducible level 1 scientific evidence.

All these studies compared two different cohorts of patients, and did not match the patients on age, gender and ISS. Furthermore, patients in the standard radiological work-up group

in these studies were not described in detail. The present study showed however, that these patients underwent total-body CT scanning after conventional imaging in 14% of the cases. In these patients, only time is a factor of importance when comparing them to patients in the immediate TBCT group. All available evidence suggests that total-body CT scanning in injured patients leads to fast and accurate diagnosis and treatment.[3, 10-13, 23-25] Previous studies showed that diagnostic work-up time was significantly longer in patients who underwent the standard radiological work-up.[12,26,27] However, the clinical relevance of speeding up the diagnostic process cannot be described based on these retrospective series.

RTS and TRISS could be calculated in 39 TBCT patients (26%) and 35 control patients (23%). RTS differed significantly between TBCT and control patients (7.55 vs. 7.84, P=0.008) as well as TRISS (0.98 vs. 0.99, P=0.017). However, patients in whom TRISS could not be calculated were more severely injured than patients in whom TRISS could be calculated. This was reflected by a higher on-scene endotracheal intubation rate (30% vs. 16%, P=0.025), a lower median GCS pre-hospital (13 vs. 15, P=0.036) and a higher median ISS (20 vs. 16, P=0.009). Age, sex, mechanism of injury, pre- and in hospital hypotension rates and in-hospital GCS were comparable between patients in whom TRISS could not be calculated and patients in whom TRISS could be calculated.

The major limitation of our study is that patients were compared retrospectively. Although matching parameters were carefully chosen and ISS is strongly related to mortality[28], there were differences in pre-hospital parameters and the incidence of serious head injuries between the groups. Preferably, we would have selected control patients based on the same inclusion criteria as TBCT patients. However, these data could not be retrieved retrospectively in a reliable manner. We therefore used matching to select a cohort of control patients that is more comparable to the patients selected in the TBCT group than would have been the case when using all control patients admitted between 2006 and 2007. This would have yielded more control patients who were not comparable to TBCT patients, for example with a lower ISS and a lower prevalence of mortality. Although it would have made the logistic regression analysis easier, there would have been more 'noise' that had to be explained by the prediction model. Furthermore, fewer variables could have been used in the prediction model since the prevalence of mortality will be lower when using all control patients. By matching, the number of confounding variables in our prediction model was reduced. This was done in other studies as well, although in those studies retrospective selection of patients was used to create groups with an ISS of 16 and higher[10] or patients who were admitted to the ICU.[22] In several studies on this topic similar differences in characteristics between study groups were found and statistical methods were used to correct for these differences.[10, 21, 22] Obviously, matching possibly only partially compensates for the difference in selection methods of TBCT patients and the subsequent regression analysis has been restricted to a limited number of predictors. Consequently, residual confounding may remain like in most observational studies.

Another limitation of the present study is that the ISS in the TBCT patients might be influenced by the more extensive classification that is made possible by the total-body CT scan.[17] This phenomenon has been described in patients with occult pulmonary contusions, in whom the median ISS was increased without significant consequences for complication rate and mortality.[29] Because the majority of control patients had a considerable number of CT scans after conventional imaging as well, we think that this effect is marginal.

To investigate the causal relationship between initial imaging and mortality in injured patients, a multicenter randomized clinical study is underway.[15] This randomized trial does not only focus on clinical outcome, but will analyse radiation dose and cost-effectiveness as well. An analysis of all these factors together is required to provide a complete overview of the advantages and disadvantages of using immediate total-body CT in the initial evaluation of injured patients.

CONCLUSION

In conclusion, this case-matched series showed that patients who underwent immediate total body CT scanning had comparable absolute mortality rates when compared with trauma patients who underwent conventional imaging and selective CT scanning. After correction for confounders, a decrease in 30-day mortality in TBCT patients was apparent.

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5

INCIDENTAL FINDINGS ON TOTAL-BODY CT SCANS IN TRAUMA PATIENTS

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Injury, 2013

ABSTRACT

Objective Total-body Computed Tomography (CT) scans are increasingly used in trauma care. Herewith the observation of incidental findings, trauma unrelated findings, is also increased. The aim of this study was to evaluate the number of incidental findings in adult trauma patients.

Methods All consecutive trauma patients that underwent total-body CT scanning between January 2009 and December 2011 were analyzed. Incidental findings were divided in three categories: category I (potentially severe condition, further diagnostic work-up is required), category II (diagnostic work-up dependent on patients' symptoms) and category III (findings of minor concern, no diagnostic work-up required).

Results There were 2248 trauma room presentations; 321 patients underwent a total-body CT scan (14.3%). In 143 patients (44.5%), 186 incidental findings were reported. There were 13 category I findings (7%), 45 category II findings (24%) and 125 category III incidental findings (67%). Overall, 18 patients (5.6%) required additional diagnostic work-up. Four patients underwent work-up by additional radiologic imaging. Three patients required further invasive work-up or treatment. Three patients were transferred to another hospital, no extended follow-up was performed. In three patients, there was no documentation of follow-up. Five patients deceased before diagnostic work-up of the incidental finding could start.

Conclusion Total-body CT scanning as part of the evaluation of trauma patients leads to a substantial amount of incidental findings. Documentation of incidental findings and their clinical consequences was incomplete. Therefore, the findings of this study have prompted us to add an item to our electronic trauma room report that obliges residents to report whether or not incidental findings are found during trauma imaging.

INTRODUCTION

Total-body Computed Tomography (CT) scanning is increasingly used as a diagnostic technique in trauma patients. The main advantage of this total-body imaging concept is a quick and complete overview of traumatic injuries in all relevant body regions (head to pelvis).[1-3] One of the most important disadvantages is the associated radiation exposure.[4,5] Another point of interest is the observation of incidental findings on total-body CT scanning. These are defined as findings that are totally unrelated to the clinician's reasons for requesting the radiological examination.[6] These incidental findings might be beneficial to patients in case of earlier detection of a malignancy. Conversely, it might result in increased patients' anxiety and health care costs in case of additional work-up for abnormalities that ultimately might not affect patients' health.[7,8]

The total amount of incidental findings on selective CT scans of one or more body regions in trauma patients varies between 34%[9] and 45%.[10,11] A recent study reported a 36% incidental findings rate on routine thoracoabdominal CT in trauma patients.[14] Only two studies evaluated incidental findings in patients that underwent a total-body CT scan as part of the initial trauma evaluation and incidental finding numbers of 50% and 53% were found.[15,16] However, indications for a total-body CT scan were not described in both studies and the clinical consequences of these incidental findings were unclear.[15]

Therefore, the aim of this study was to evaluate the percentage of incidental findings and their clinical consequences in a cohort of adult trauma patients who underwent total-body CT scanning.

PATIENTS AND METHODS

Patient selection

All consecutive trauma patients admitted to our academic Level I trauma center that underwent total-body CT scanning between January 2009 and December 2011 were included in this study. All patients fulfilling the in- and exclusion criteria listed in Table 1 underwent immediate total-body CT scanning. Prior conventional imaging was not an exclusion criterion for the present study.

Total-body CT

All patients were evaluated on a sliding gantry 64-slice CT-scanner (Sensation 64, Siemens Medical Solutions, Forchheim, Germany) located in our trauma resuscitation room. Total-body CT scanning consisted of a two-step total-body acquisition (from vertex to pubic symphysis) starting with Head and Neck Non-Enhanced CT with arms alongside the body. Directly after repositioning the arms alongside the head for the second part of the scan covering chest,

abdomen and pelvis, a split-bolus intravenous contrast protocol was injected (Optiray® 350 125 ml Pre fill, Covidien Mallinckrodt, Cincinnati, USA). The reconstruction thickness was 5mm head and 1 mm bone kernel for the brain, 1mm bone kernel for the cervical spine and 3mm soft tissue and bone kernel for the torso.

Table 1 Criteria for immediate total-body CT scanning

Trauma patients with the presence of one of the following vital parameters:
o respiratory rate >29/min or <10/min;
o pulse >120/min;
o systolic blood pressure < 100 mmHg;
o estimated exterior blood loss > 500 ml;
o Glasgow Coma Score ≤ 13;
o abnormal pupillary reaction on site.
OR Trauma patients with one of the following clinically suspicious diagnoses:
o fractures from at least two long bones;
o flail chest, open chest or multiple rib fractures;
o pelvic fracture;
o unstable vertebral fractures;
o spinal cord compression.
Trauma patients not receiving total-body CT scanning:
o known age ≤18 years;
o known pregnancy;
o referred from another hospital;
o any patient who is judged to be too unstable to undergo a CT scan and requires (cardiopulmonary) resuscitation or immediate operation.

Data collection

All trauma room patients were registered in a prospective database. A cohort that underwent total-body CT scanning was selected and data were collected anonymously.

Double-reading of radiologic imaging by the resident on call and by a senior radiologist with expertise in trauma is common practice in our center. By protocol, if previous radiology reports are present they are compared with current CT findings. The presence of incidental findings in the radiology report and the clinical consequences were determined by an unblinded investigator. Clinical consequences were defined as actions (i.e. diagnostic work-up or treatment) following the incidental finding. Information was extracted from computerized hospital databases containing admission and discharge letters, radiological reports, surgery reports and pathology reports.

The Institutional Review Board evaluated the study protocol and declared that the need for informed consent was waived. Data collection was done solely in our level-1 trauma center. Due to privacy reasons, there was no extended follow-up.

Incidental finding in categories

Incidental findings were divided in three categories: category I is an incidental finding that is a potentially severe condition, further diagnostic work-up is required. Work-up consisted of additional blood tests, consultation of other specialties, radiologic imaging or invasive diagnostic procedures. In category II diagnostic work-up is dependent of patients' symptoms and category III are findings of minor concern for which no diagnostic work-up is required. The definitions of the categories were comparable to categories described in previous studies[9,14,15] and combine the potential severity of the abnormalities found with the respective clinical consequences.

The following incidental findings were excluded: degenerative joint diseases, stenotic atherosclerotic vessel disease, sinusitis, age-related brain cerebral atrophy and signs of earlier operation. These conditions were considered clinically known or irrelevant for the research question, in accordance with previous studies.[9,14] CT findings which were already known from previous (radiological) examinations were excluded.

Statistical analysis

Descriptive statistics with SPSS software (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.) was used to describe the data. For continuous data, mean and standard deviation (parametric data) or median and interquartile ranges (non-parametric data) were calculated.

RESULTS

There were 2248 trauma room presentations between 2009 and 2011 of which 321 patients underwent a total-body CT scan (14%) during trauma survey. Patient characteristics of the study population are shown in Table 2. In 143 patients (45%), 186 incidental findings were found. Incidental findings per body region according to category are depicted in Figure 1. Most incidental findings were located in the abdomen.

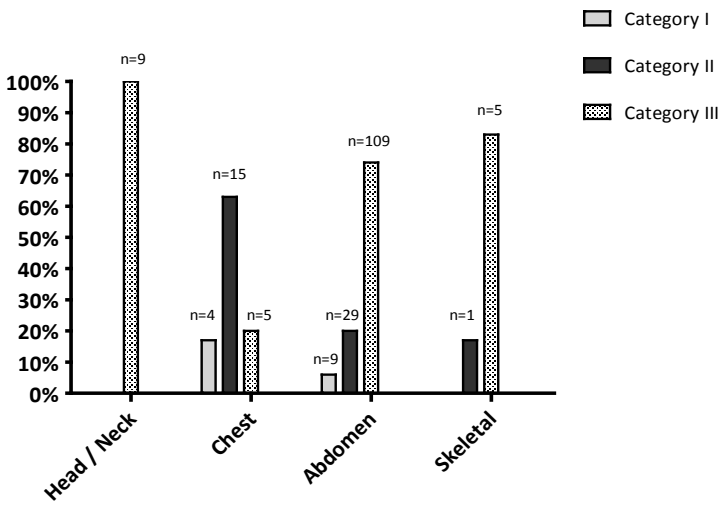
Table 2 Patient characteristics

	n=321
Age (years)	43.8 (21.4)*
Men	231 (71.7%)
Blunt trauma	308 (95.7%)†
Mechanism of injury	
motor vehicle collision	116 (36.0%)
fall from height	90 (28.0%)
bicycle accident	42 (13.0%)
pedestrian accident	20 (6.2%)
penetrating	12 (3.7%)†
other	43 (13.0%)
ISS	22 (IQR=10-29)
Multitrauma patients (defined as ISS ≥16)	226 (70.2%)
Hospital stay (days)	9 (IQR=2-22.3)

Data are number (%) or median (interquartile range (IQR)) unless otherwise indicated. Abbreviations: ICU= Intensive Care Unit; ISS= Injury severity score.

* Mean (SD) † Two patients had combined blunt and penetrating trauma

Figure 1 Incidental findings per body region



Category I, potentially severe condition that requires further diagnostic work-up; category II, diagnostic work-up dependent of patients' symptoms; category III, findings of minor concern, no diagnostic work-up required

Table 3 shows the incidental findings of category I (potentially severe condition, further diagnostic work-up required) and their respective interventions and final diagnoses (n=13). Three patients underwent work-up by radiologic imaging (ultrasound and CT) and one or more visits to a medical specialist. One patient required further invasive work-up (lymph node resection with a final diagnosis of disseminated non-seminoma testicular carcinoma; Figure 2) and two patients underwent surgery (endovascular repair of an aneurysm of the abdominal aorta and a laparoscopic adnex extirpation). One patient with a 2.9 cm large adrenal mass was, on his own request, referred to a specialist in another hospital; no further follow-up was obtained. Three patients deceased before diagnostic work-up and three patients were lost to follow-up. All patients that were lost to follow-up had category I findings with the advice for further diagnostic work-up in the correspondence, but there was no documentation of follow-up in the medical chart.

Table 3 Incidental findings of Category I (potentially severe condition that requires further diagnostic work-up, n=13)

Incidental finding	Intervention	Final diagnosis
Pulmonary mass (n=3)	Deceased before intervention (n=2) Follow-up by CT (n=1)	- Mass decreased, no malignancy
Mediastinal lymphadenopathy (n=1)	Lymph node resection	Non-seminoma testicular tumor
Liver mass (n=1)	Deceased before intervention	Autopsy: suspicious for HCC
Aneurysm abdominal aorta > 5cm (n=1)	Endovascular repair	Abdominal aneurysm
Pancreatic mass suspect for main-duct type IPMN (n=1)	MRI was advised	Lost to follow-up*
Renal mass suspect for malignancy (n=1)	Follow-up by CT	Mass decreased, no malignancy
Hydronephrosis (n=1)	Follow-up was advised	Lost to follow-up†
Adrenal mass (n=2)	Follow-up was advised	Referral to other hospital Lost to follow-up‡
Ovarian cyst > 5cm (n=1)	Laparoscopic adnex extirpation	Epithelial cyst
Irregular aspect uterus and adnex (n=1)	Follow-up by ultrasonography	No irregularities diagnosed

Abbreviations: HCC, hepatocellular carcinoma; IPMN, intraductal papillary mucinous neoplasm.

*In the ICU letter, a visit to the surgical outpatient clinic was advised. There was no documentation of follow-up in the medical chart.

† The radiologist recommended an adrenal protocol CT scan. There was no documentation of follow-up in the medical chart.

‡ The radiologist recommended follow-up. In the ICU letter the incidental finding was mentioned, but after transfer to another hospital, there was no documentation of follow-up.

Figure 2 In a 27-year old male, right paratracheal and para aortic lymphadenopathy was found incidentally on a total-body CT scan that was made during trauma work-up. After lymph node resection, pathology showed metastasis of a non-seminoma testicular tumor.

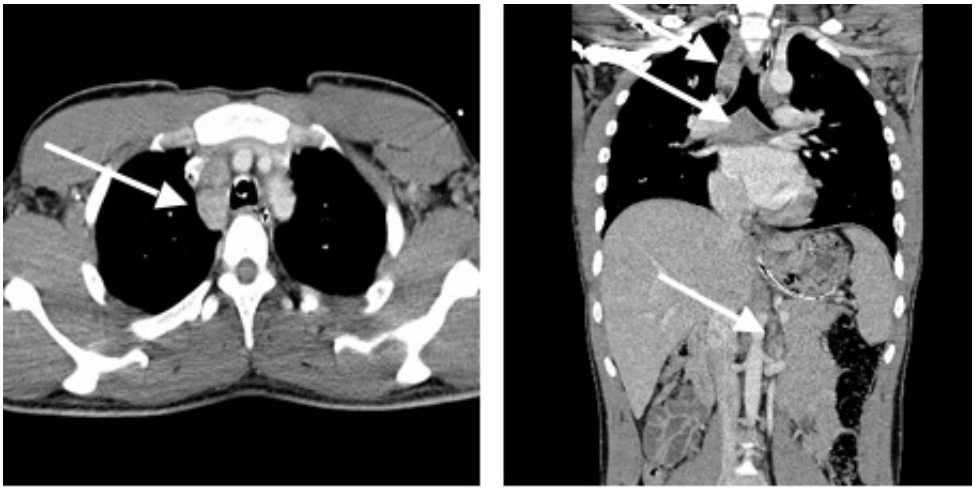


Table 4 Incidental findings of Category II (diagnostic work-up dependent of patients' symptoms, n=45)

Pleural plaques (n=6)	Diaphragmatic hernia (n=5)
Pulmonary emphysema (n=3)	Umbilical hernia (n=1)
Cardiomegaly (n=3)	Renal pelvic dilatation (n=1)
Slight mediastinal lymphadenopathy (n=2)	Renal atrophy (n=1)‖
Calcified mediastinal lymph nodes (n=1)*	Adrenal hyperplasia (n=1)
Aneurysm abdominal aorta <5cm (n=1)*	Adrenal adenoma (n=2)
Fatty liver infiltration (n=4)	Infrarenal aortic dissection (n=1)
Liver enlargement (n=1)†	Disc herniation L5-S1 (n=1)
Hyperdense liver lesions (n=1)‡	Prostatic hypertrophy (n=1)
Cholecystolithiasis (n=6)	Uterine lipoleiomyoma (n=1)
Common bile duct dilatation (n=2)	

Diagnostic or therapeutic consequences:

* Patient deceased before (diagnostic or therapeutic) intervention.

† In the ICU discharge letter the incidental finding was mentioned, follow-up by additional blood tests was advised and the patient was transferred to another hospital.

‡ Follow-up by MRI was advised by the radiologist. No further documentation.

‖ Renal ultrasound performed. Final diagnosis: congenital renal atrophy or atrophy due to nephropathy.

Incidental findings of category II (diagnostic work-up dependent of patients' symptoms) are outlined in Table 4 (n=45). In 40 patients, no further diagnostic work-up was done. In one patient work-up by radiologic imaging was done (renal ultrasound). Two patients deceased before diagnostic work-up and two patients were lost to follow-up. In one of the patients that were lost to follow-up, hepatomegaly was detected. In the ICU letter the incidental finding was mentioned and follow-up by additional blood tests was recommended. Subsequently, the patient was transferred to another hospital. The other patient had liver lesions that required follow-up by MRI as advised by the radiologist. There was no documentation of follow-up in the medical chart.

Table 5 Incidental findings of Category III (findings of minor concern, no diagnostic work-up required, n=128)

Brain	**Abdomen**
Brain calcifications (n=1)	Hypodense noduli liver parenchyma (n=3)
Brain cysts (n=4)	Liver cyst (n=24)
Spica of sinus maxillaris and mastoid (n=1)	Liver hemangioma (n=7)
	Hypodense splenic nodule (n=3)
Neck	Calcifications in the spleen (n=1)
Thyroid nodule (n=2)	Splenic hemangioma (n=1)
Retrosternal thymus rest (n=1)	Accessory spleen (n=1)
	Fatty changes of the pancreas (n=1)
Chest	Calcifications in the pancreas (n=2)
Non-specific small pulmonary nodus (n=3)	
Aortic calcification (n=2)	Diverticulosis coli (n=15)
	Calcified mesenterial lymph nodes (n=1)
Skeletal	
Vertebral hemangioma (n=3)	Follicle cyst (n=1)
Bone cyst (n=2)	Corpus luteum cyst (n=1)
	Renal angiomyolipoma (n=1)
	Horse-shoe kidney (n=1)
	Renal cyst (n=39)
	Thinning of the renal cortex (n=1)
	Renal calcifications (n=2)
	Adrenal cyst (n=1)
	Slightly enlarged adrenal gland (n=1)
	Incidentaloma adrenal gland (n=1)
	Adrenal myolipoma (n=1)

Incidental findings of category III (findings of minor concern, no diagnostic work-up required) are shown in Table 5 (n=125). None of the patients with incidental findings in category III underwent further diagnostic work-up as was expected. All incidental findings located in craniofacial or in the neck region were of category III.

Based on definitive diagnosis the prevalence of malignant tumors in the total trauma population was 0.6%.

DISCUSSION

This study shows that the percentage of incidental findings in a cohort of adult trauma patients that underwent total-body CT scanning is 45%. Most incidental findings were located in the abdomen. Overall, 18 patients (6%) received complementary diagnostic work-up or therapeutic intervention because of a potentially severe condition. In three patients, there was no documentation of follow-up found in the medical chart despite recommendation for follow-up of their category I incidental finding.

Although there are several studies describing incidental findings on selective CT scans, few studies addressed the topic in total-body CT scanning. One study reported on incidental findings in a large cohort of over 3000 patients, however, consequences of the incidental findings were not described.[15] In another study, incidental findings in 304 patients were described including clinical consequences.[16] Strength of the present study is that a considerable amount of prospectively registered patients was included and that all incidental findings and their consequences are described.

Strikingly, an important number of patients that required complementary diagnostic work-up, had insufficient documentation of follow-up in their medical chart (3 out of 18 patients). Poor documentation has been described previously.[9-13] It was shown that less than 20% of the patients with an incidental finding of moderate to severe concern had evidence of follow-up.[11] More recently, Paluska et al.[9] found that only in 48% of the incidental findings requiring attention before discharge, there was chart documentation of treatment, follow-up or referral.

Insufficient documentation of incidental findings and effectuation of diagnostics and/or follow-up have ethical and potential legal ramifications. Therefore, the findings of this study have prompted us to add an item to our electronic trauma room report that obliges residents to report whether or not incidental findings are found during trauma imaging. Furthermore, which actions should be taken and by whom should also be reported on this electronic report. Since this information is now required to be described in the admission papers, it is therefore also recorded in the discharge letter to the general practitioner. We believe that this dedicated

protocol that is incorporated into our trauma algorithm, will make residents more aware of the presence of incidental findings and subsequent actions to be taken. That dedicated attention results in improved capture, documentation and management of incidental findings have been shown previously.[17]

The detection of a disease in an earlier stage could be a possible advantage related to incidental findings. A recent study showed that the number of CT scans per trauma patient has more than doubled over six years.[18] There is a risk that more radiologic imaging is done than strictly needed and subsequently more incidental findings are found, while benefits for the patient remain uncertain. This is supported by Ekeh et al.[19] who found 35% incidental findings on trauma abdominal CT scans, while in 75% of the patients no concomitant traumatic injuries were present. Munk and colleagues[10] found that physicians were more likely to detect an incidental finding than a traumatic injury on abdominal CT scans for trauma in a general trauma population.

Overdiagnosis, in terms of the detection of a condition that would otherwise not cause symptoms or death, might lead to further diagnostic tests that are not strictly necessary[6]. Patients might be overexposed to ionising radiation with subsequent life-time risk for developing cancer. Currently, medical imaging is responsible for 50% of the total radiation exposure to the population in the United States.[20] It is estimated that approximately 29 000 future cancers every year could be the result of past CT scan use.[21] Furthermore, invasive diagnostic procedures following an incidental finding have their own subsequent risks for complications and might increase health care costs extensively.[6,8] In addition to the physical hazards, increased concern awaiting results of diagnostic tests might unnecessarily affect patients. Whether the advantages of this total-body imaging concept outweigh the disadvantages for trauma patients, is currently under investigation in the REACT-2 trial.[22]

Limitations

The retrospective part of the study design is a limitation of this study. Preferably, we would have included information concerning all pre-existent findings that were already known by the patient before trauma evaluation. To reduce this problem we have checked previous documentation in our own hospital but this does not rule out known diseases in other institutions. Even more important is the verification of all clinical consequences. It is possible that we have missed clinical consequences, because of poor documentation and because patients were not followed after discharge from the hospital.

The reason not to perform a follow-up also based on information from other institutions was based on our widespread (inter)national distribution of our trauma population and on former experiences in trauma follow-up studies.

Third, it is possible that not all incidental findings were described in the radiological reports. When reviewing a total-body CT scan in trauma setting, the focus of the resident radiology is on possible life-threatening traumatic injuries and therefore less relevant incidental findings might be missed. However, the double-reading system by a senior radiologist that is applied in our hospital should minimize the risk for missing incidental findings.[23]

CONCLUSION

Total-body CT scanning as part of the evaluation of trauma patients leads to a substantial amount of incidental findings. The majority of findings does not require further diagnostic work-up or therapeutic intervention although some life-threatening findings were detected.

Documentation of incidental findings and their clinical consequences was incomplete. Therefore, the findings of this study have prompted us to add an item to our electronic trauma room report that obliges residents to report whether or not incidental findings are found during trauma imaging. We suggest that other institutions consider doing the same.

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6

RADIATION EXPOSURE BEFORE AND AFTER THE INTRODUCTION OF A DEDICATED TOTAL-BODY CT PROTOCOL IN MULTI TRAUMA PATIENTS

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ABSTRACT

Objective Total-body CT scanning in trauma patients is being increasingly used in trauma assessment. One of the major disadvantages of CT scanning is the amount of radiation exposure involved. The aim of this study was to assess the number of radiological investigations and their associated radiation exposure in multi trauma patients before and after the introduction of a total-body CT protocol as a primary diagnostic tool.

Methods The Trauma Registry was used to identify trauma patients admitted to our Level-1 trauma center in 2008 (pre-TBCT protocol) and 2010 (post-TBCT protocol). Consecutive patients with an Injury Severity Score of ≥16 were included. Patients aged 16 or under, referrals from other hospitals and patients with specific low-energy injury mechanisms were excluded. Subsequent effective doses were estimated from literature and from dose calculations.

Results 301 patients were included, 150 patients pre- and 151 post-introduction of the TBCT protocol. Demographics were comparable. In 2008, 20% of severely injured patients underwent a total-body CT scan, compared with 46% of the patients in 2010. Trauma room radiation doses for conventional radiographs were significantly higher in 2008, while doses for CT-scans were significantly lower. The total effective dose of trauma room radiological investigations was 16 milliSieverts (mSv) in 2008 vs. 24 mSv in 2010 (P=0.223). The overall effective dose during the total hospital admission was not significantly different between 2008 and 2010 (20 mSV vs. 24 mSV, P=0.509).

Conclusion After the introduction of a dedicated TBCT protocol the TBCT rate was more than doubled. Although this increased the CT induced trauma room radiation dose, the overall radiation dose during total hospital admission was comparable between patients in 2008 and 2010.

INTRODUCTION

Computed tomography (CT) is a valuable tool in the assessment of trauma patients.[1,2] It is a fast and highly accurate modality for the identification of various injuries[3-5] and it enables a rapid response to life-threatening problems.[6] Therefore, total-body CT scanning, comprising a CT scan of the head, neck, chest, abdomen and pelvis, is becoming increasingly popular.[7] However, the main disadvantage of CT scanning is the considerable amount of radiation exposure.[8]

Several studies have compared radiation doses between pre- and post-total-body CT scan (TBCT) protocol cohorts.[7,9] A recent study[10] has shown that after the introduction of a TBCT scanning protocol, the risk of receiving a higher radiation dose during the trauma evaluation was increased. An increase in radiation exposure both during the first 24 hours in the hospital[9] as well as during the total hospital stay[7] was shown. This was mainly attributed to an increase in the use of CT scans.[7,9,11] However, in all these studies the number of multi trauma patients (Injury Severity Score [ISS] ≥16) was relatively low. In addition, severely injured patients will more often undergo a total-body CT scan and radiation exposure is higher than in patients with a lower ISS.[12-14]

The aim of this study was to assess the amount of radiation exposure that severely injured patients were exposed to before and after the introduction of a dedicated total-body CT scan protocol. It was our hypothesis that multi trauma patients admitted during a period when a dedicated TBCT protocol was in force received a higher dose of radiation in the trauma room, but a lower total dose of radiation throughout the hospital admission period compared with the doses received by patients admitted before the introduction of the TBCT protocol.

PATIENTS AND METHODS

Since 2009, a policy of carrying out immediate total-body CT scanning has been in force at our level-1 trauma center. All patients fulfilling criteria regarding life-threatening vital parameters on admission and who were clinically suspected of having severe injury or certain injury mechanisms immediately underwent a TBCT scan instead of conventional imaging supplemented by selective CT scanning (Table 1). Before 2009, multi trauma patients were evaluated in accordance with the ATLS® principles using primary conventional imaging (X-rays and ultrasonography) and selective CT scanning on indication. During the study period, the trauma evaluation setting, equipment and the imaging techniques did not differ.

Data extraction

The Dutch Hospital Trauma Registry, a prospective national database of all trauma patients kept up to date by trained data managers, was used to identify trauma patients admitted in 2008

(pre-total-body CT protocol) and 2010 (post-total-body CT protocol). Patients with an Injury Severity Score of 16 and higher were selected for inclusion in the study. Patients aged 16 or under, referrals from other hospitals and patients with specific, low-energy injury mechanisms (i.e. drowning, carbon monoxide intoxication, water intoxication, hanging or burn injury) were excluded.

The numbers and types of radiologic examination carried out were extracted retrospectively from computerized hospital databases. Double data entry was done independently by two authors. Any discrepancies in the number or type of imaging were resolved by discussion between the reviewers.

Table 1 Criteria for total-body CT-scanning in trauma patients

Trauma patients with the presence of one of the following vital parameters:
o respiratory rate >29/min or <10/min;
o pulse >120/min;
o systolic blood pressure < 100 mmHg;
o estimated exterior blood loss > 500 ml;
o Glasgow Coma Score ≤ 13;
o abnormal pupillary reaction on site.
OR patients with one of the following clinically suspicious diagnoses:
o fractures from at least two long bones;
o flail chest, open chest or multiple rib fractures;
o pelvic fracture;
o unstable vertebral fractures;
o spinal cord compression.
Trauma patients not receiving total-body CT scanning:
o known age <18 years;
o known pregnancy;
o referred from another hospital;
o any patient who is judged to be too unstable to undergo a CT scan and requires (cardiopulmonary) resuscitation or immediate operation.

Effective dose calculations

After ascertaining the numbers and types of radiologic examination, we calculated the subsequent doses of radiation in accordance with standard effective doses. We assigned an effective dose value to every type of radiological investigation, instead of to every individual patient to exclude possible effect on dose estimates due to differences in patient weight and scan length between the cohorts. Dose catalogues published by Mettler et al.[15] were used to determine the effective doses for X-ray examinations and interventional radiology procedures

(Table 2). X-rays of clavicle and shoulder were regarded as X-rays of the extremities, pelvic ala and obturator X-ray views were regarded as pelvic X-rays and sternum and rib X-rays were regarded as chest X-rays. The dose for X-rays of the thoracolumbar transition is not described in Mettler et al.[15], and was therefore estimated as the average for a thoracic spine X-ray and a lumbar spine X-ray (1.25 milliSieverts (mSv)).

Table 2 Effective doses for conventional X-ray imaging

Examination	Average effective dose (mSv)
Skull	0.1
Chest	0.02
Cervical spine	0.2
Thoracic spine	1
Lumbar spine	1.5
Abdomen	0.7
Acetabulum	0.7
Pelvis	0.6
Extremity (other)	0.001

Abbreviations: mSv, milliSievert.

As average dose values for the CT protocols used in a trauma setting were not readily available in literature, we calculated representative radiation doses for the various CT scans based on optimized trauma CT protocols at our level-1 trauma center (Table 3). Doses of CT scans of the extremities were excluded in the analysis. To calculate effective doses, we used the ImPACT CT Dosimetry spreadsheet (www.impactscan.org/ctdosimetry.htm).

Fluoroscopy is excluded from the present study since those were not used for diagnostic examinations for treatment decision which is the scope of this paper.[15]

Table 3 Effective doses for Computed Tomography procedures

Examination	Average effective dose (mSv)
Total-body	24
Brain	1.8
CTA brain	2.5
Sinuses	0.6
Mastoid	0.36
Cervical spine	3
CTA carotids	4.4
Chest	5.1
CTA chest	3.4
Thoracic spine	12
Shoulder	1
Abdomen	11
Upper abdomen	6.5
Kidney	11
Lumbar spine	12
Pelvis	4.5

Abbreviations: CTA, Computed Tomography Angiography; mSv, milliSievert.

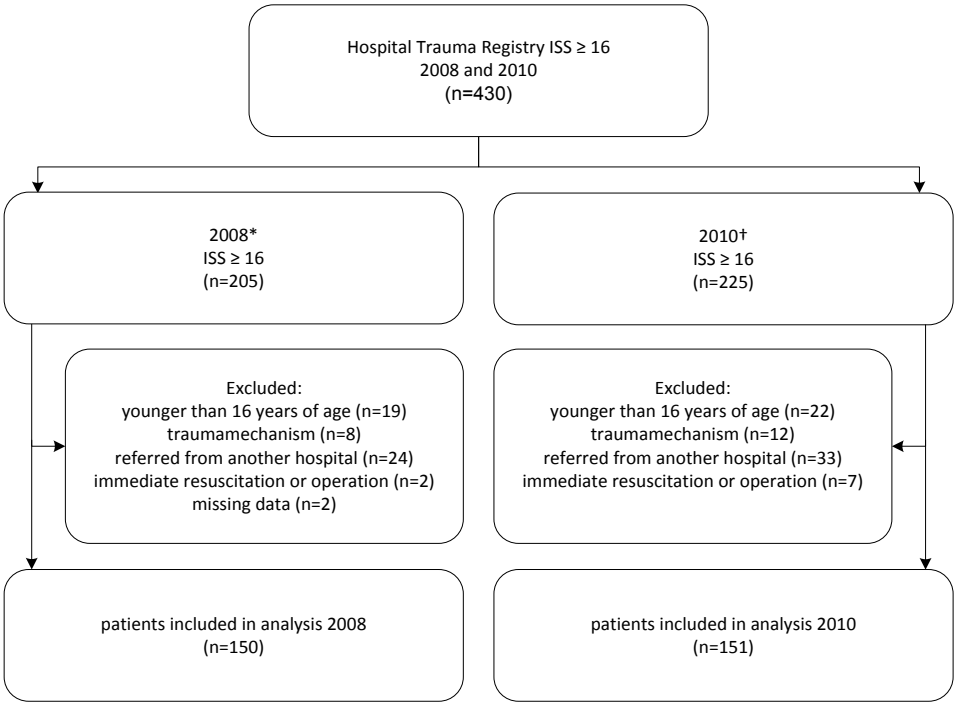
Statistical analysis

Continuous data are presented as medians and interquartile ranges (IQR). Categorical data are presented as frequencies and percentages. To compare dichotomous outcomes, the Chi-square test was used. Continuous outcomes with a skewed distribution were analyzed by means of the Mann-Whitney U test. A P-value < 0.05 was considered to be statistically significant. Statistical analyses were performed with PASW statistics for Windows (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.)

RESULTS

There were 301 patients who fitted the criteria for the study, 150 patients before (2008) and 151 patients after (2010) the introduction of the TBCT scan protocol. A flowchart of the selection process is depicted in Figure 1.

Figure 1 Flowchart of the patient selection process



* 2008 cohort: pre-total-body CT scan protocol
† 2010 cohort: post-total-body CT scan protocol

Patient demographics and clinical outcomes were comparable between the two groups of patients (Table 4). A TBCT scan was performed less in 2008 than in 2010 (20% vs. 46%, P<0.001).

The number of radiological examinations is presented in Table 5. More conventional radiographs and fewer CT scans were carried out in 2008 than in 2010, both in the trauma room and throughout the total hospital admission period.

Table 4 Patient demographics

	2008 n=150	2010 n=151	P-value
Age (years)	40.5 (29-62.3)	42 (26-62)	0.965
Sex (male)	111 (74%)	104 (68.9%)	0.325
Blunt trauma	142 (94.7%)	139 (92.1%)	0.363
Total-body CT scan	30 (20%)	70 (46.4%)	<0.001
Injury Severity Score (ISS)	22 (18-27)	25 (17-29)	0.383
ISS categories			0.404
16-24	84 (56%)	73 (48.3%)	
25-49	63 (42%)	75 (49.7%)	
50-75	3 (2%)	3 (2%)	
Body region with AIS ≥3			
chest	87 (25.8%)	73 (21%)	0.135
abdomen	37 (11%)	38 (10.3%)	0.788
extremities	63 (18.7%)	64 (18.4%)	0.919
Blood transfusion	54 (36%)	53 (35.1%)	0.870
ICU stay (days)	2 (0-4)	2 (0-4)	0.506
Hospital stay (days)	10 (4-22)	9 (4-18)	0.295
Mortality rate			0.816
no mortality	134 (89.3%)	138 (91.4%)	
24h	8 (5.3%)	6 (4%)	
30 days	8 (5.3%)	7 (4.6%)	

All data are number (%) or median (interquartile range).
Abbreviations: AIS, Abbreviated Injury Scale; ISS, Injury Severity Score, CT, Computed Tomography; ICU, Intensive Care Unit.

Table 6 shows the calculated radiation doses in 2008 and 2010 for patients in the trauma room and during hospital admission (trauma room excluded and trauma room included). Trauma room doses for conventional radiographs were significantly higher in 2008 while doses for CT-scans were significantly lower. The total amount of trauma room radiation dose did not differ significantly between 2008 and 2010 (16 mSv (IQR=12-25) vs. 24 mSv (IQR=12-25), P=0.223). The calculated amount of radiation dose during hospital admission (trauma room excluded) was marginally different between 2008 and 2010 (1.8 mSv (IQR=0-9) vs. 1.8 mSv (IQR=0-5), P=0.043). Overall, the total radiation dose during hospital admission did not differ between 2008 and 2010 (20 mSV (IQR=13-32) vs. 24 mSV (IQR=13-30), P=0.509).

Table 5 Number of radiological examinations performed before (2008) and after (2010) the introduction of a TBCT protocol

	2008 n=150	2010 n=151	P-value
Trauma room			
X-rays	8.5 (3-11)	3 (0-9)	*<0.001*
CT scans*	3 (2-4)	4 (2-5)	0.012
Hospital admission			
X-rays	4 (1-9.3)	2 (0-7)	*0.045*
CT scans*	0.5 (0-1)	1 (0-2)	0.604
Angiography†	3 (1-5)	2 (1.5-6)	0.402
Total			
X-rays	13 (8-18)	9 (2-14)	*<0.001*
CT scans*	3 (2-5)	5 (3-6)	0.016

All data are number (%) or median (interquartile range).

*A total-body CT is calculated as 4 CT-scans (head/chest/abdomen/pelvis).

†2008 cohort: abdominal angiography n=12, head and/or neck angiography n=1, thoracic angiography of pulmonary artery or aorta n=5, angiography pelvis minor n=2, angiography of iliac artery n=3.

†2010 cohort: abdominal angiography n=8, thoracic angiography of pulmonary artery or aorta n=3, angiography of iliac artery n=6.

Table 6 Radiation dose before (2008) and after (2010) the introduction of a TBCT protocol

	2008 n=150	2010 n=151	P-value
Trauma room			
X-ray radiation dose	3.5 (0.6-8.1)	0.6 (0-6.2)	*<0.001*
CT radiation dose	9.9 (4.8-19.1)	16.8 (4.8-24)	*0.005*
Total radiation dose	16.1 (12.3-24.6)	24 (11.7-24.6)	0.223
Hospital admission			
X-ray radiation dose	0.1 (0-1.7)	0 (0-0.5)	*0.011*
CT radiation dose	0 (0-5.1)	0 (0-3.6)	0.838
Total radiation dose	1.8 (0-9.2)	1.8 (0-4.8)	*0.043*
Total radiation dose hospital admission	20.1 (12.9-31.9)	24 (12.9-29.9)	0.509

All data are medians (interquartile range).

Radiation doses are in milliSievert.

DISCUSSION

In 2008, 20% of the severely injured patients underwent a total-body CT scan, compared with 46% of these patients in 2010. Although in 2010, patients received a higher radiation dose on CT scanning in the trauma room, as hypothesized by the present study, the total trauma room radiation dose was not significantly higher. Furthermore, the total hospital admission radiation dose did not significantly differ between patients in 2008 and 2010.

These findings are partially in accordance with others in the current literature. One previous study shows that the number of CT-scans more than doubled over six years, generating more radiation exposure[9]. However, only diagnostic imaging during the first 24 hours of hospitalization has been included. The outcome that radiation dose from CT scanning in the trauma room was higher is also shown by our study. However, our study also shows that the total amount of radiation dose received by our study groups during hospital admission was comparable.

Another study in a substantial cohort of 1,280 patients shows an increase in the proportion of patients who received a radiation dose of more than 20 mSv after the introduction of a total-body CT scan protocol.[10] The dose of 20 mSv was based on the theoretical risk of cancer, which rises above one in 1,000.[10] A limitation of this study was that radiological examinations in the trauma room were included and repeat examinations were excluded from the analysis. This amount of more 20 mSv was also found in the present study. However, the most important finding was that the overall radiation dose did not significantly differ throughout total hospital admission. The introduction of a dedicated TBCT protocol does not seem to increase the risk of radiation-induced risk of cancer.

Although this study shows that there is no increase of total hospital admission radiation dose after the introduction of a dedicated TBCT protocol for trauma evaluation, we would like to emphasise the importance of knowledge on radiation exposure. Several studies show that this knowledge by non-radiologist but also by radiologists is poor. By presenting this data, we would like to raise awareness of radiation exposure.[16,17]

One potential limitation of the present study was that no differentiation was made between patients with a blunt and penetrating trauma. Normally, different imaging and evaluation strategies are used for these two populations. Since only seven patients in 2008 and 12 patients in 2010 presented with a penetrating trauma, we felt that a separate analysis was not meaningful. Another limitation was that data on radiological examinations were retrieved retrospectively although risk of entry errors was minimized by means of double data entry by two independent authors. Finally, due to the retrospective study design, rather than giving the precise doses of radiation exposure for each individual patient, the effective doses were

calculated. We chose this model, because it makes data less dependent on the specific CT-scanner settings and different approaches to scan protocols, i.e. number of passes through the body. In addition, if individual doses had been calculated, certain patient characteristics such as weight could be an unconsciously confounder as data on weight (and thus the distribution between 2008 and 2010) were not present in the trauma registry nor could they reliably be obtained at presentation.

The strengths of our study are that a considerable number of multi trauma patients with similar characteristics is included, double data entry was done to minimize risk of data entry errors and a clear and reproducible description of the effective dose estimates was given.

CONCLUSION

We conclude that the TBCT rate and CT-induced radiation dose during trauma room evaluation of multi trauma patients were higher after the introduction of a dedicated TBCT protocol. However, the overall radiation dose during the total hospital admission was comparable for these severely injured trauma patients.

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7

A MULTICENTER, RANDOMIZED CONTROLLED TRIAL OF IMMEDIATE TOTAL-BODY CT SCANNING IN TRAUMA PATIENTS (REACT-2)

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ABSTRACT

Objective Computed tomography (CT) scanning has become essential in the early diagnostic phase of trauma care because of its high diagnostic accuracy. The introduction of multi-slice CT scanners and infrastructural improvements made total-body CT scanning technically feasible and its usage is currently becoming common practice in several trauma centers. However, literature provides limited evidence whether immediate total-body CT leads to better clinical outcome then conventional radiographic imaging supplemented with selective CT scanning in trauma patients. The aim of the REACT-2 trial is to determine the value of immediate total-body CT scanning in trauma patients.

Methods The REACT-2 trial is an international, multicenter randomized clinical trial. All participating trauma centers have a multi-slice CT scanner located in the trauma room or at the Emergency Department (ED). All adult, non-pregnant, severely injured trauma patients according to predefined criteria will be included. Patients in whom direct scanning will hamper necessary cardiopulmonary resuscitation or who require an immediate operation because of imminent death (both as judged by the trauma team leader) are excluded. Randomization will be computer assisted. The intervention group will receive a contrast-enhanced total-body CT scan (head to pelvis) during the primary survey. The control group will be evaluated according to local conventional trauma imaging protocols (based on ATLS® guidelines) supplemented with selective CT scanning. Primary outcome will be in-hospital mortality. Secondary outcomes are differences in mortality and morbidity during the first year post trauma, several trauma work-up time intervals, radiation exposure, general health and quality of life at 6 and 12 months post trauma and cost-effectiveness.

Discussion The REACT-2 trial is a multicenter randomized clinical trial that will provide evidence on the value of immediate total-body CT scanning during the primary survey of severely injured trauma patients. If immediate total-body CT scanning is found to be the best imaging strategy in severely injured trauma patients it could replace conventional imaging supplemented with CT in this specific group.

Trial registration ClinicalTrials.gov (NCT01523626).

INTRODUCTION

Injuries are the cause of 5.8 million deaths annually which accounts for almost 10% of global mortality.[1] Among adults aged 15–59 years the proportion of injuries as cause of death is even higher, ranging from 22% to 29%.[1] Injuries, whether unintentional or intentional, may have devastating effects on the lives of individuals and poses a great burden on public-health budgets.[2] This burden may even increase in the future, since the World Health Organization (WHO) predicted a 28% increase in global deaths due to injury between 2004 and 2030.[1]

Specialized trauma centers all over the world provide initial trauma care and diagnostic work-up of trauma patients. This work-up is standardized and frequently based on the Advanced Trauma Life Support (ATLS®) guidelines which include a fast and priority-based physical examination as well as screening radiographs supplemented with selective Computed Tomography (CT).[3] ATLS® guidelines advise to routinely perform X-rays of chest and pelvis and Focussed Assessment with Sonography for Trauma (FAST) in trauma patients. X-rays of the spine and extremities are performed based on clinical suspicion during the secondary survey. Whether or not to perform CT scanning following conventional imaging is defined less clearly in the ATLS® guidelines and depends upon national guidelines and local protocols.

In recent years CT has become faster, more detailed and more available in the acute trauma care setting. CT shows high accuracy for a wide range of injuries[4-7] which is reflected by a low missed diagnosis rate.[5,8-10] Hence, the conventional radiological work-up according to the ATLS may not be the optimal choice of primary diagnostics anymore. Furthermore, severely injured patients frequently require secondary CT scanning of many parts of the body after conventional imaging. Modern multi-detector CT scanners (MDCT) can perform imaging of the head, cervical spine, chest, abdomen and pelvis in a single examination (total-body CT scanning). The past few years this total-body imaging concept gained popularity as a possible alternative to the conventional imaging strategy. With the use of immediate total-body CT scanning in trauma patients, rapid and detailed information of organ and tissue injury becomes available and a well-founded plan for further therapy can be made.

In the past, CT scanners were located in the radiology department, frequently even on another floor than the emergency department (ED) were the trauma patient is admitted. The past assumption that total-body CT scanning in severely injured trauma patients is too time consuming may no longer be held, since an increasing number of trauma centers have a CT scanner available at the ED or even in the trauma room itself.[11,12] Several studies evaluated time intervals associated with total-body CT usage in severely injured patients.[4,5,8,13-18] Time intervals focussed on are scanning time, time to all diagnosis known and time in the ED. Some studies compare different scanning protocols[19-21], some evaluate the effects of a total-body CT scan in

one group trauma patients[5,8,9], while others make a comparison in two cohorts trauma patients, one evaluated with an immediate total-body CT scan and one evaluated with ATLS based imaging protocols and selective CT scanning.[22-25] Although these studies are incomparable with respect to design, CT scanners used, diagnostic work-up protocols and trauma populations[26], the main conclusion is clear. Total-body CT scanning in trauma patients is not as time consuming as was once expected and may even be time saving compared to conventional imaging protocols supplemented with selective CT.

The most important question remains whether immediate total-body CT scanning can be translated into improved clinical outcome. A recent study in 4621 trauma patients reported a significant increase in the probability of survival for patient given immediate total-body CT scanning compared with conventional imaging strategies supplemented with selective CT scanning.[25] However, since the study was retrospective in nature, no correction for all confounding variables could have been made. Patients who underwent immediate total-body CT scanning were on average more severely injured than those who did not receive total-body CT scanning. Differences between participating centers and protocols used for diagnostic work-up were not described. Whether the positive effect in survival in patients who underwent total-body CT scanning can be attributed solely to the total-body CT scan itself, remains therefore unclear.

Although literature provides limited evidence for the usage of an immediate total-body CT scan in the work-up of trauma patients, more and more trauma centers encourage and are implementing immediate total-body CT scanning in the diagnostic phase of primary trauma care. Since the burden of total-body CT scanning in terms of costs and radiation dose is at least controversial[20,27,28], the advantage of performing an immediate total-body CT scan should be proven in high quality studies resulting in high level evidence in order to make its implementation justifiable.

In order to assess the value of immediate total-body CT scanning in severely injured trauma patients, the Academic Medical Center (AMC) in Amsterdam, the Netherlands, has initiated an international multicenter randomized controlled trial. Severely injured patients, who are thought to benefit the most from a total-body imaging concept, will be included. Such a trial has never been done before and is crucial to provide evidence whether or not the usage of immediate total-body CT scanning in the diagnostic phase of primary trauma care is justifiable.

METHODS/DESIGN

Study objectives

The primary objective is to determine the effects of immediate total-body CT scanning during the primary trauma survey on clinical outcomes compared to patients who are evaluated with standard conventional Advanced Trauma Life Support (ATLS®) based radiological imaging. The secondary objectives are to assess the effects of total-body CT scanning on long term clinical outcomes, quality of life, clinically relevant time intervals in the early phase of trauma care and the differences in treatment strategies used.

Study design

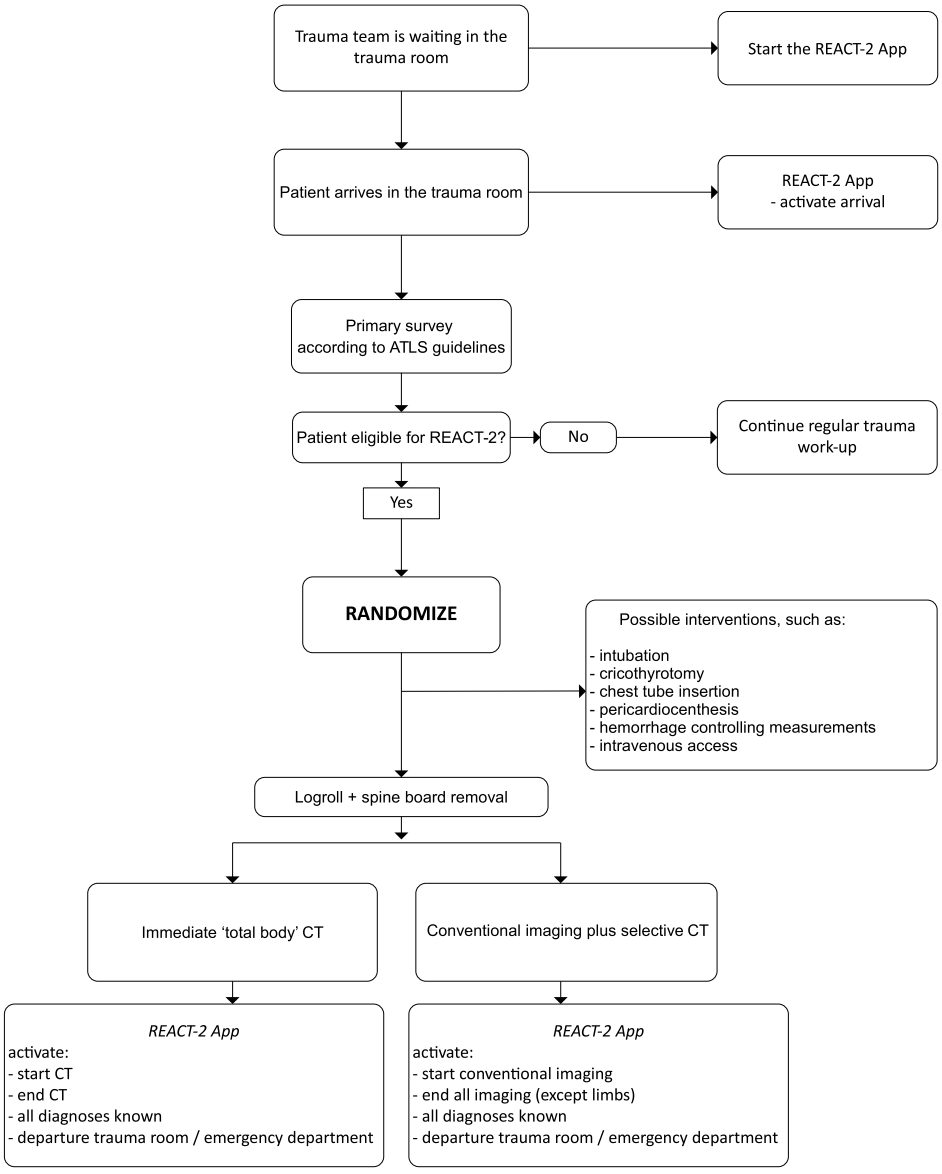
The REACT-2 trial is an international, multicenter randomized clinical trial in six high-volume trauma centers that will compare the effects of immediate total-body CT scanning in severely injured trauma patients with conventional imaging protocols.

Setting

In total four trauma centers in The Netherlands, one Swiss and one American trauma center will participate in the REACT-2 trial. All participating hospitals are level-1 trauma centers with a multi-slice CT scanner located in the trauma resuscitation room or at the ED.

When a patient arrives in the trauma room a brief report of the pre-hospital circumstances, medical assessment and clinically suspected injuries is presented to the trauma team leader by the ambulance personnel. The initial evaluation of trauma patients will be done according to the ATLS® guidelines for the primary survey. Potential life-saving interventions during the primary survey and before any imaging include securing the airway by intubation or performing a cricothyrotomy, chest tube insertion, pericardiocenthesis or taking hemorrhage controlling measurements such as applying a pelvic binder or external pressure on bleeding sites to (temporarily) stabilize the vital functions. Usually, peripheral intravenous access is taken care of by the ambulance personnel, but if not, at least one intravenous catheter will be inserted before radiologic imaging takes place. Based on information received from the ambulance personnel and the findings during primary survey, the trauma team leader decides on the eligibility of the patient to participate in the trial. If the patient is found to be eligible randomization takes place. Figure 1 depicts the study flow chart.

Figure 1 Study flow chart REACT-2 trial



The intervention group will receive a total-body CT scan from head to pelvis. In the intervention group conventional radiography of the torso and FAST will be completely omitted. The CT protocol consists of a two-step whole-body acquisition (from vertex to pubic symphysis) starting with Head and Neck Non Enhanced CT (NECT) with arms alongside the body. The preferred technique for the second complementary scan is a split-bolus intravenous contrast directly after

repositioning of the arms alongside the head, and this second scan covers thorax, abdomen and pelvis. Participating centers however are free to choose their own technique as long as intravenous contrast is given for the chest and abdominal part of the total-body CT.

The control group will be evaluated according to a conventional trauma protocol with selective CT scanning. The REACT-2 trial has been designed to maximize the applicability of the trial's results to usual care settings. Therefore, the technical details of the CT scanning done in the control group are not specified and participating centers follow their own protocols. Indications for the selective CT scanning however are pre-defined based on the combined local protocols of the participating centers. These standardized protocols provide a basis for the comparison of the two imaging approaches.

Study population

All non-pregnant trauma patients aged 18 years and older having life-threatening (respiratory, circulatory or neurologically) conditions with compromising vital parameters, with clinical suspicion on specific injuries or with specific injury mechanisms are included. Patients in whom the scanning will hamper necessary (cardiopulmonary) resuscitation or who require an immediate operation because of imminent death (both as judged by the trauma team leader) are excluded. Detailed in- and exclusion criteria are summarized below:

Inclusion criteria

Trauma patients with the presence of life-threatening vital problems defined as at least one of the following:

- respiratory rate ≥30 min of ≤10/min;
- pulse ≥120/min;
- systolic blood pressure ≤ 100mmHg;
- estimated exterior blood loss ≥ 500 ml;
- Glasgow Coma Score ≤ 13;
- Abnormal papillary reaction on site.

OR

Patients with one of the following clinically suspicious diagnoses:

- flail chest, open chest or multiple rib fractures;
- severe abdominal injury;
- pelvic fracture;
- unstable vertebral fractures/spinal cord compression;
- fractures from at least two long bones.

OR

Patients with one of the following injury mechanisms:

- fall from height (>3 m or >10 ft);
- ejection from the vehicle;
- death occupant in same vehicle;
- severely injured patient in same vehicle;
- wedged or trapped chest/abdomen.

Exclusion criteria

Trauma patients with one of the following characteristics will be excluded:

- known age <18 years;
- known pregnancy;
- referred from another hospital;
- clearly low-energy trauma with blunt injury mechanism;
- penetrating injury in 1 body region (except gun shot wounds) as the clearly isolated injury;
- any patient who is judged to be too unstable to undergo a CT scan and requires (cardiopulmonary) resuscitation or immediate operation because death is imminent according to the trauma team leader in mutual agreement with the other leading care givers.

Endpoints

The primary outcome criterion for this trial is in-hospital mortality.

Secondary parameters focus on additional clinical consequences for the patients and cost-effectiveness and cost-utility:

- mortality (24-h, 30-day and 1-year mortality);
- morbidity (complications and total number of (re-)interventions and re-admissions up to 6 months post trauma; transfusion requirements, length of ICU stay and number of ventilation days);
- several time intervals during initial evaluation (time of arrival, time to CT, scanning time, time to diagnosis and time in the ED);
- radiation exposure;
- quality of life 6 and 12 months after the trauma as recorded by completing the EuroQol-6D;
- general health 6 and 12 months after the trauma as recorded by completing the HUI-3;

Economic parameters/endpoints:

- total costs of imaging during the initial/index hospital stay;
- total direct and indirect medical and non-medical costs during the first half year posttrauma;
- quality adjusted life-years (QALY's).

Randomization

If a patient is eligible for the trial the diagnostic imaging pathway for initial assessment in the trauma resuscitation room will be determined by randomization. The randomization will be performed immediately after inclusion at computers located in the trauma room of the participating hospitals. Randomization will be performed using a 'one-click' computer program on a 1:1 basis per hospital with varying block sizes of 2, 4, 6, 8, 10 and 12. The trauma team will be directly informed on the outcome of the randomization so that imaging can be started. A standardized case record from (CRF) will be used. This CRF is totally web-based via a secured internet module.

Sample size calculation and data analysis

A previous study reported a reduction in mortality from 15% to 8.6% with total-body CT scanning as the single diagnostic procedure during trauma evaluation as compared to historical control data.[29] Analysis on the large German polytrauma registration database performed by Huber-Wagner et al. showed a significant reduction in the 24-h mortality in patient who underwent immediate total-body CT compared to the conventional group (10% vs. 12%, P=0.038).[25] Historical AMC data show a mortality rate of 12% for trauma patients matching the current trial inclusion criteria. Based on the combination of the AMC data and the participation of the other trauma centers with comparable trauma populations, it is expected to find a reduction in mortality from 12% to 7%. The detection of such a difference requires 539 patients per group using a power of 80% and a two-sided alpha of 5%. Based on the historical and estimated data of the participating centers the inclusion period will take about 1.5 years and the follow-up period will take an additional year.

The main analyses of primary and secondary outcomes will be conducted for all randomized patients according to the result of the randomization (intention-to-treat). Data are expressed as percentages for categorical data, as mean and standard deviation (SD) for normally distributed numerical data and as median, range, and, where appropriate, inter-quartile range (IQR=25 to 75%) for non-normally distributed numerical data.

The following subgroups will be used for subgroup analysis:

- multitrauma patients (defined as Injury Severity Score (ISS) ≥16);
- severe traumatic brain injury patients (defined as admission Glasgow Coma Scale (GCS) ≤8 and an Abbreviated Injury Score (AIS)-head of ≥3);
- penetrating versus blunt trauma.

A P-value less than 0.05 is considered statistically significant. If appropriate, predictive values between variables are calculated. Predictive values in continuous outcome variables are assessed using a multivariate regression model, and binary outcome measures are assessed using a

multivariate logistic regression model. In case of binary outcome measures, predictive values are expressed as Odds Ratio's (OR) with 95% Confidence Intervals (CI). Data are analyzed using the Statistical Package for the Social Sciences (SPSS) version 18.0 SPSS Inc., Chicago, IL.

Economic evaluation and cost analysis

Total-body CT scanning will be evaluated economically from a societal perspective against a conventional diagnostic strategy consisting of X-ray, FAST and selective CT scanning according to the ATLS® guidelines. Cost-effectiveness analyses will be performed with the costs per patient alive and costs per patient alive without serious morbidity as outcome measures. Additionally, a cost-utility analysis will be done with the cost per QALY as outcome measure. Incremental cost-effectiveness ratios will be calculated, expressing the extra costs per (i) extra patients alive, (ii) extra patients alive and without serious morbidity, and (iii) additional QALY. Sampling variability will be accounted for by (bias-corrected and accelerated) non-parametric bootstrapping. Sensitivity analyses will be directed at applied QALY algorithms (generic, country-specific; uniform, linear, curvilinear interpolations between measurements), unit costs of major cost components, and the (country-specific) friction period in case of production loss. Subgroup analyses will be performed by the predefined subgroups. The time horizon for the cost-effectiveness analysis will be six months following trauma. Because of this time horizon, no discounting will take place.

The economic evaluation will take all direct and indirect medical and non-medical costs into account. The direct and indirect medical costs include the costs of initial trauma care, ICU-care and care at the general ward during the index admission - including all diagnostic and therapeutic procedures – as well as the costs of repeat hospital admissions, other intramural care like rehabilitation and extramural care during the first 6 months post trauma. Direct and indirect non-medical costs of, respectively, out-of-pocket expenses and production loss during the first 6 months will also be estimated. Volume data will be collected by case report form, institutional administrative databases and by patient questionnaires at 3 and 6 months, depending on the cost category. The patient questionnaire will be derived from the Dutch Health and Labour Questionnaire and adapted for international use. Unit costing will be based on activity based costing and hospital ledger data concerning the major diagnostic procedures in this trial. Unit costing of other health care components will be based on available national guidelines. In case of absence of national guidelines in specific countries, available unit costs from abroad will be recalculated using Organisation for Economic Co-operation and Development (OECD) purchasing power parities. Out-of-pocket expenses will be estimated as supplied by the patients. Indirect costs of production loss will be calculated according to the Dutch perspective by following the friction cost method, while applying the most recent friction cost period known at the time of analysis. Costs will be calculated for the base year 2012. Unit costs of other base years will be price-indexed.

Safety monitoring

An independent Data and Safety Monitoring Board (DSMB), consisting of three members (2 physicians and 1 clinical epidemiologist), is installed for this trial. On regular intervals, this committee will review accumulating trial data and provide advice on the conduct of the trial to the trial leader and Steering Committee. The DSMB will focus both on safety and effectiveness data. Standard Operating Procedures (SOP) will be used with respect to the schedule and format of DSMB meetings and with respect to the format and timing of presenting data. The DSMB can recommend the Steering Committee to terminate the trial when there is clear and substantial evidence of harm.

The role of the DSMB is to perform an interim review of the trial's progress including updated figures on main outcomes and safety data. This review would include, but not be restricted to, the following:

- monitor compliance with the protocol by participants and investigators;
- monitor evidence for treatment differences in the main efficacy outcome measures;
- monitor evidence for treatment harm (e.g. SAEs, deaths);
- decide whether to recommend that the trial continues to recruit participants or whether recruitment should be terminated either for everyone or for some treatment groups and/or some participant subgroups;
- suggest additional data analyses;
- monitor compliance with previous DSMB recommendations;
- consider the ethical implications of any recommendations made by the DSMB;
- assess the impact and relevance of external evidence as supplied by the Chief Investigator.

The DSMB will evaluate these safety and efficacy parameters at regular intervals. After 275 (25%), 550 (50%) and 700 (65%) included patients, non-blinded interim-analyses for evaluation of safety rules will be performed. No formal stopping rules based on statistical criteria alone will be used. The DSMB decides after evaluation of all necessary interim data whether the trial will be continued or terminated. Other investigators, designated by the Board of Direct of the AMC to control the trial will have the authority to gain insight in all the confidential data relevant for the trial as well.

Ethics

This trial is conducted in accordance with the principles of the Declaration of Helsinki[30], the Medical Research Involving Human Subjects Act (WMO) and 'Good Clinical Practice' guidelines. The Medical Ethical Committee of the Academic Medical Center in Amsterdam has approved the protocol on January 6 2011. The Ethical Committees of the participating centers approved for local feasibility.

To participate in a research project the subjects must be volunteers and informed participants according to ethical principles stated in the Declaration of Helsinki. However, the acute life-threatening situation of severely injured trauma patients hinders a considered decision. Neither a legal guardian nor a legal representative of the patient can make a decision because of the time pressure or because they simply do not arrive in time. A temporary waiver of informed consent during randomization and the consecutive diagnostic phase during trauma survey was approved by the Medical Ethical Committee of the Academic Medical Center in Amsterdam. In all cases informed consent will be asked afterwards from the patient or the legal guardian/ representative of the patient, as soon as reasonably possible.

DISCUSSION

The need for prospective studies to measure the effect of immediate total-body CT scanning in trauma care has been stressed recently by several authors.[8,22,23,25,29] Retrospective studies have shown the possible benefits in time and outcome of immediate total-body CT scanning in trauma patients. The next step is to compare its usage to the current best imaging strategy according to ATLS guidelines in a prospective trial.

The primary question that needs to be answered is whether immediate total-body CT scanning in severely injured trauma patients decreases mortality and significant morbidity when compared to conventional imaging strategies supplemented with CT. Therefore, randomization is within the hospital, ensuring that a comparison between imaging protocols is made per hospital instead of between hospitals. The design of the trial is multi-centered, with participating centers in The Netherlands, Switzerland and North America. This design assures that differences in trauma populations, trauma mechanisms and workflow in different parts of the world are taken into account as well. This is important to make sure that if an effect on outcome is seen that this can solely be attributed to the usage of a total-body CT scan.

The in- and exclusion criteria assure that only potentially severely injured trauma patients are included and over triage is minimized. Especially severely injured patients are thought to benefit the most from fast and detailed information that becomes available with total-body CT scanning. Selecting the right patients for immediate total-body CT scanning is therefore crucial. Since the excluded trauma patients will be registered as well, final analysis will show whether the chosen inclusion criteria led to an appropriate selection of patients. Furthermore, severely injured patients are those patients in whom the radiation dose may be justifiable since their possible life-threatening injuries require accurate treatment as fast as possible. Trauma patients are exposed to a great amount of radiation and it is well known that CT scanning is a significant contributor to iatrogenic radiation exposure.[31] The mean effective dose received by trauma patients evaluated by conventional imaging protocols supplemented with CT scanning

was found to be 22.7 milliSievert (mSv).[32] A single total-body CT scan accounts for 14–21 milliGray (mGy), which in medical X-ray studies is equal to mSv.[31] However, cumulative doses for all the radiological examinations undertaken during hospitalization may be much higher.[33] The long-term effects of the radiation exposure are based upon estimations, but the most concerning is an increased cancer risk. For a single total-body CT examination the estimated lifetime attributable cancer mortality risk is thought to be around 0.08%.[31]

After conventional imaging in terms of X-rays and ultrasound has been finished, the trauma leader has to decide whether or not selective CT should take place. The ATLS® guidelines provide some decision rules but to some extent it is susceptible to individual judgment. Experience of the trauma leader and local infrastructures may influence these decisions. Furthermore, the randomization between total-body CT and conventional imaging supplemented with CT within each center holds the risk of a learning curve experienced by trauma leaders. If the trauma leader suspects detecting more injuries with a total-body CT scan than was expected on clinical grounds, performing selective CT scanning in the conventional arm could become more easily accessible and may lower the possible differences in outcome between the study groups. That is why the indication for selective CT scanning in the conventional arm are pre-defined, based on combined local protocols of the participating centers. The standardization of the conventional arm will lower the aforementioned risks.

This trial aims to determine the optimal diagnostic strategy for severely injured trauma patients in the ED. If immediate total-body CT scanning is found to be the best imaging strategy in severely injured trauma patients it could replace conventional imaging supplemented with CT in this specific group. This will probably minimize the total diagnostic work-up time of the initial trauma evaluation. How this reflects in outcome needs to be analyzed in this trial. Furthermore, severely injured patients are already likely to receive selective CT scanning after conventional imaging according to ATLS® guidelines or according to local trauma protocols. Segmented CT scanning in these patients, added to the conventional work-up, will result in a high total radiation dose because of overlapping radiation fields. It could therefore even be possible that an immediate total-body CT results in a lower total effective radiation dose compared to the conventional work-up with selective CT scanning.[27]

The trial not only focusses on clinical outcome in terms of mortality and morbidity. Since radiation exposure and cost-effectiveness will be taken into account as well, the REACT-2 trial will provide a detailed overview of considerations that should be taken into account when discussing the efficacy of immediate total-body CT scanning in trauma patients. The large sample size will make sure that results are reliable and can be generalized to all international trauma populations and centers.

Conclusion

The REACT-2 trial is an international multicenter randomized clinical trial (ClinicalTrials.gov/NCT01523626) to compare immediate total-body CT scanning during the primary survey of severely injured trauma patients with conventional imaging strategies supplemented by selective CT scanning.

Prospective

The REACT-2 inclusion has started in April 2011. Results are expected in mid 2014.

Abbreviations

ATLS, Advanced Trauma Life Support; AIS, Abbreviated Injury Score; AMC, Academic Medical Center; ED, Emergency Department; FAST, Focused Assessment with Sonography for Trauma; GCS, Glascow Coma Scale; ICU, Intensive Care Unit; mGy, Milligray; ISS, Injury Severity Score; mSv, milliSievert; REACT-2, Randomized study of Early Assessment by CT scanning in Trauma patients –2; CT, Computed Tomography.

Competing interests

J.C. Sierink, MD, is a Ph.D.-student at the Trauma Unit Department of Surgery, employed by the AMC Medical Research B.V., and supported by an unrestricted grant from ZonMw, the Netherlands organisation for health research and development (grant number: 171102023). All authors declare that they have no competing interests.

Authors' contributions

JCS drafted the manuscript, TPS and JCG co-authored the writing of the manuscript. All authors participated actively in the design of the trial and critically appraised the manuscript. All authors read and approved the final manuscript.

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8

IMMEDIATE TOTAL-BODY CT SCANNING VERSUS CONVENTIONAL IMAGING AND SELECTIVE CT SCANNING IN SEVERE TRAUMA PATIENTS: A RANDOMIZED CONTROLLED TRIAL (REACT-2 TRIAL)

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Submitted

ABSTRACT

Background: Recent literature suggests a survival benefit for trauma patients when they are evaluated with total-body Computed Tomography (TBCT) scanning during the initial trauma evaluation. However, level-1 evidence is lacking.

Methods: In this multicenter clinical trial, we randomly assigned 541 trauma patients to immediate TBCT scanning and 542 patients to the standard workup with conventional imaging supplemented with selective CT scanning. Trauma patients having compromized vital parameters, clinical suspicion of life-threatening injuries or severe injury mechanisms were eligible. The primary endpoint was in-hospital mortality. Secondary endpoints were radiation exposure, clinically relevant time intervals, missed injuries and direct medical costs.

Findings: The in-hospital mortality rate was similar in both groups (TBCT 15.9% vs. standard 15.7%, P=0.923). There was a limited absolute increase in median radiation dose during the total hospital stay in the TBCT group, but substantially more patients in the standard workup group received a lower effective radiation dose, as reflected by the wide interquartile ranges (IQR) (21.0mSv [IQR=20.9-25.2] versus 20.6mSv [IQR=11.8-27.6], P<0.001). Imaging time in the trauma room was decreased in the TBCT group (30 min vs. 37 min, P<0.001). The number of missed injuries found during the tertiary survey was similar in both groups (45 [8.8%] vs. 53 [10.1%], P=0.448). The medical costs were €24,967 (95% CI: €21,880– €28,752) for the TBCT group and €26,995 (95% CI: €23,326–€30,908) for the standard workup group (P=0.439).

Interpretation: Total-body CT scanning was safe, shortened the imaging time and did not increase the medical costs, but it did not improve survival, and most patients in the standard workup group received a lower radiation dose.

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BACKGROUND

Total-body computed tomography (TBCT) scanning is increasingly used in the primary evaluation of trauma patients, and is performed according to Advanced Trauma Life Support (ATLS)® guidelines.[1] CT scanning is accurate and safe for the detection of traumatic injuries.[2] A significant advantage of the total-body imaging concept as compared to the standard workup with X-rays, ultrasound and selective CT scanning is the rapid and complete overview of life-threatening traumatic injuries. Time benefits in favor of TBCT scanning compared with the standard workup,[3-6] changes in treatment associated with the TBCT scanning[7] and potential survival benefits[3,8-13] have been described previously.

A potential disadvantage of TBCT scanning of trauma patients is the increased radiation exposure.[14,15] As a side effect, incidental (i.e., trauma-unrelated) findings are more frequently found with TBCT scanning.[16-18] Despite the lack of level-1 scientific evidence for the use of TBCT scanning in the evaluation of trauma patients,[2,19,20] an increasing number of trauma centers have incorporated this imaging strategy in their daily practice.[6,13,21,22] The TBCT scan could be used as a supplemental tool to the standard radiologic imaging or even as a total replacement, without prior conventional imaging (e.g., X-rays and ultrasound).

Most previously performed studies retrospectively included a specific cohort of patients (e.g., polytrauma patients defined as patients with an Injury Severity Score (ISS) of 16 and above).[3,13] Because the ISS is calculated retrospectively at discharge, this parameter is not available in daily clinical practice and cannot be used as a triage method for the selection of severely injured patients. Therefore, intrinsic methodological limitations and the risk of selection bias are confounders in these studies. The need for a randomized clinical trial was highlighted[3] and was the primary conclusion of all systematic reviews.[2,23-27]

We conducted this randomized clinical trial of early assessment with CT scanning in trauma patients (REACT-2) to examine the effect of immediate TBCT scanning as part of the primary evaluation of severe trauma patients on in-hospital mortality, and compared it with that of the standard workup employing conventional imaging supplemented with selective CT scanning. Secondary objectives included radiation exposure, clinically relevant time intervals, missed injuries and direct medical costs of the institutionalized care associated with immediate total-body CT scanning.

METHODS

Study design and oversight

REACT-2 was designed as an international, randomized controlled multicenter trial in which immediate total-body CT scanning in severe trauma patients was compared with a standard workup with conventional imaging supplemented by selective CT scanning. The design of the REACT-2 study has been previously described (ClinicalTrials.gov: NCT01523626).[28] The study was approved by the Medical Ethics Committees at all participating centers (MEC 10/145).

Study population

Eligibility criteria were chosen with the aim of enrolling a trauma population with potentially severe injuries. Those with compromised vital parameters, clinical suspicion of life-threatening injuries or severe injury mechanisms were eligible. The complete list of inclusion and exclusion criteria is available in the Appendix, Table 1.

Randomization and study treatment

At the initial presentation in the trauma room and in the presence of a temporary waiver of informed consent, eligible patients were identified and randomly assigned in a center-stratified 1:1 ratio to either immediate total-body CT scanning without prior conventional imaging or to the standard workup. Potential life-saving interventions during the primary survey and prior to imaging included securing the airway by intubation, obtaining intravenous access, chest tube insertion, pericardiocentesis or taking hemorrhage control measures. Indications for selective CT scanning in the standard workup group were predefined according to local protocols (Appendix, Table 2). The multidetector CT scanner was located in the trauma room or in a room adjacent to the Emergency Department (ED). Subsequent medical care was provided according to local protocols based on current international trauma care standards.

At the earliest possible moment after the trauma workup, the patient or his legal representative was informed about the REACT-2 trial. Written informed consent was requested. All patients for whom written informed consent could be obtained were sent 3 questionnaires (EuroQol-6D, HUI-3 and a questionnaire derived from the Dutch Health and Labour Questionnaire for cost-effectiveness analysis)[28] at 3, 6 and 12 months post trauma. Patients for whom written informed consent could not be obtained, despite all efforts, were included in the intention-to-treat analysis, except for outcomes based on patient questionnaires (n=170; approved by the Medical Ethics Committee and the Dutch Central Committee on Research Involving Human Subjects). Data for the 3-, 6- and 12-month follow-up were prospectively collected from clinical and outpatient reports in the hospital databases. If no information could be obtained from this database, the patient and/or their general practitioner were contacted by telephone by one of the authors or research nurses. If a patient was transferred to another hospital, data from this hospital were also included in the analyses.

Radiological imaging

The protocol for the intervention (TBCT) group consisted of a two-step acquisition (from vertex to pubic symphysis) without gantry angulations, starting with a non-enhanced CT of the head and neck (NECT) with arms alongside the trunk. The second scan covers the chest, abdomen and pelvis. The preferred technique for the second scan was a split-bolus intravenous contrast imaging directly after raising the arms alongside the head.[29]

The standard radiologic trauma workup was performed according to ATLS® guidelines.[1] Chest and pelvic x-rays and Focussed Assessment with Sonography for Trauma (FAST) ultrasound imaging were performed during the ATLS® based primary survey. Following further assessment and resuscitation during the secondary survey, a selective CT-scan could be made of individual body regions with segmented acquisition of the respective body regions.

Endpoints

The primary endpoint was in-hospital mortality, defined as mortality during the index hospital admission after trauma (including patients who were transferred to another hospital following initial admission at one of the participating sites). Secondary endpoints were clinically relevant time intervals during trauma survey, radiation exposure, missed injuries and direct medical costs.

The cumulative radiation dose was defined as the sum of all effective doses from all radiologic imaging strategies (e.g. x-rays and CT scans), expressed in milliSievert (mSv) and calculated for all radiologic examinations performed in the trauma room and for the complete index admission. The radiation dose was estimated based on the dose catalogue of Mettler et al.[30] With respect to the radiation dose, X-rays of the clavicle were regarded as X-rays of the extremities; X-rays of the face and dental panoramic orthopantomography were regarded as X-rays of the skull; and a retrograde urethrogram was regarded as a pelvic X-ray. The dose for X-rays of the thoracolumbar transition was not provided by Mettler, and was therefore estimated as the average for a thoracic spine X-ray and a lumbar spine X-ray (1.25 mSv). Because average doses for the CT protocols used in a trauma setting were not readily available from the literature, we calculated representative radiation doses for single-pass CT scans of various body regions based on optimized trauma CT protocols at one of the study sites (i.e. AMC, Amsterdam, see Appendix, Table 2).[31] This trauma resuscitation room has a sliding gantry 64-slice CT-scanner (Sensation 64, Siemens Medical Solutions, Forchheim, Germany) with a multifunctional, radiolucent trauma resuscitation table. Doses of CT scans of the extremities were excluded from the analysis. To calculate effective doses, we used the ImPACT CT Dosimetry spreadsheet (www.impactscan.org/ctdosimetry.htm). Fluoroscopies were excluded because they were not used for diagnostic examinations leading to treatment decisions, which was the limit of the scope of our study.

The direct medical costs were assessed for Dutch patients only (89.3%) and included the costs for all diagnostic and therapeutic procedures in the trauma room, ICU and general ward

during the index admission. We further included the costs of inpatient and outpatient hospital consultations, repeat hospital admissions and diagnostic and therapeutic procedures during the 6 months of follow-up. Costs for a stay in a nursing home or rehabilitation center (other than rehabilitation in the index hospitals) were excluded from this analysis. Data on health care volume in the Dutch index hospitals (for all hospitalisations) were gathered uniformly from the hospital information systems. Unit costs were expressed in euros for the base year 2013; unit costs from other calendar years were price indexed using the national general consumer price indices as published by Statistics Netherlands.[32]

Definitions

Hypotension was defined as a systolic blood pressure below 90 mmHg upon arrival at the trauma room.[33] Traumatic brain injury patients were defined as having a Glasgow Coma Score below 9 at presentation and an Abbreviated Injury Scale head score of 3 or above. Polytrauma patients were defined as patients with an Injury Severity Score (ISS) of 16 or above. Trauma-Injury Severity Score (TRISS) was used to calculate the probability of survival (coefficients for blunt trauma: b0=-0.4499, b1=0.8085, b2=-0.0835 and b3=-1.7430. Coefficients for penetrating trauma: b0=-2.5355, b1=0.9934, b2=-0.0651, b3=-1.1360).[34]

Clinically relevant time intervals were defined as imaging time, time to diagnosis of life-threatening injuries and total time spent in the trauma room. Time intervals were prospectively registered by the trauma team (on a PC or tablet) starting immediately after the patient entered the trauma room. Imaging time was defined as the time from arrival in the trauma room until the end of imaging in the trauma room. Time to diagnosis was defined as the time at arrival to the time all life-threatening injuries were diagnosed according to the trauma team leader, in accordance with the radiologist.

A Serious Adverse Event (SAE) was defined as a life-threatening event during scanning. Every SAE was reported to the research coordinator and the Medical Ethics Committee within 24 hours.

Post-randomization exclusions were defined as patients who were included by mistake because they did not fulfill the inclusion criteria as assessed by a member of the study group as soon as possible after the moment of inclusion. When a mistake was suspected, the trauma team leader and the research investigator at the specific sites were contacted. In consultation with these persons, the decision was made whether a patient should be regarded as a post-randomization exclusion.

Missed injuries were defined as injuries not detected during the primary trauma survey and were prospectively registered by research staff (research nurses and clinical investigators).

Median length of stay (LoS) during total hospital admission was based on data from admitted patients only. Intensive Care Unit (ICU) LoS and ventilation days were calculated for patients admitted to the ICU.

Complications were classified according to the Clavien-Dindo Classification for surgical patients.[35]

Statistical analysis

The detection of a difference in mortality of 5% with a power of 80% and a two-sided alpha of 5% required 539 patients per group. Details of the power analysis have been described previously.[28]

The statistical analyses were performed by the authors and independently by a clinical epidemiologist not involved in the trial. The continuous data with a normal distribution are expressed as means and standard deviation, whereas the non-normally distributed data are presented as medians with interquartile ranges. Independent sample t-tests and Mann-Whitney U Tests were used to compare the continuous data, and the chi-squared test and Fisher's Exact test were used to compare the categorical variables. A P-value of less than 0.05 was considered statistically significant.

The primary analyses were performed according to the intention-to-treat principle. Per-protocol analyses, excluding crossovers (i.e. patients who received the opposite intervention to which they had been allocated), were also performed. Subgroups were specified in advance (polytrauma and severe traumatic brain injury patients) and were also analyzed.

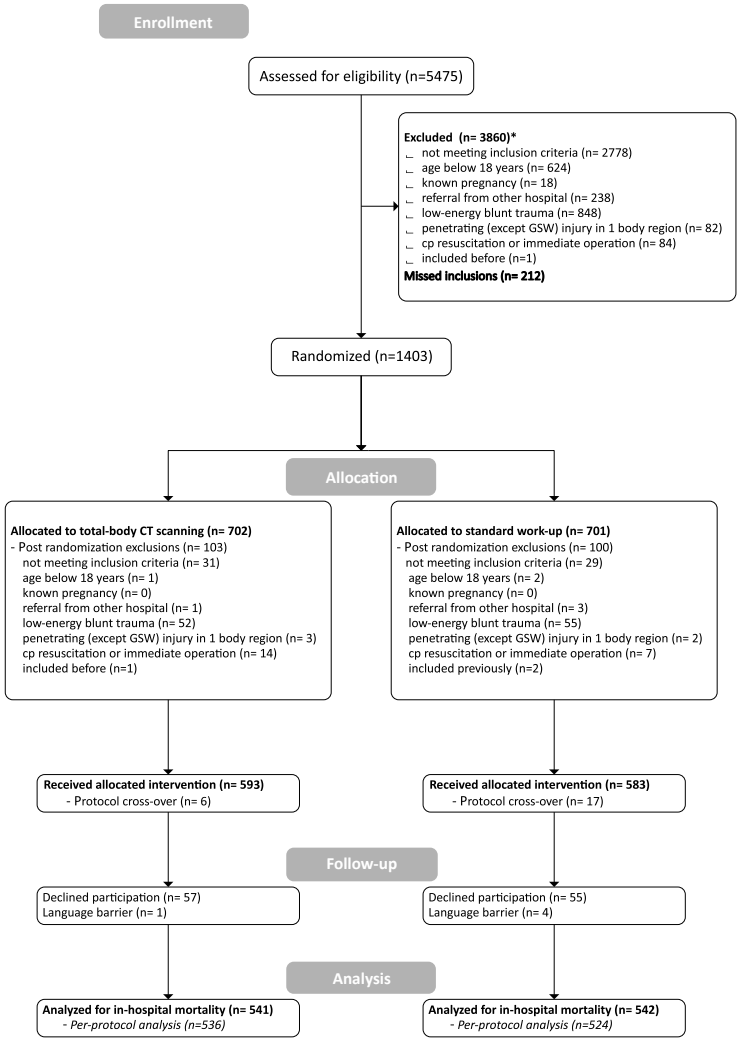
Differences in health effects and costs between TBCT scanning and the standard workup of trauma patients were assessed by calculating the 95% confidence intervals for the mean differences after correction for bias and using accelerated non-parametric bootstrapping, drawing 1,000 samples of the same size as the original sample separately for each group and with replacement.[36]

After 275 (25%), 550 (50%) and 700 (65%) patients were included, non-blinded interim analyses for the evaluation of safety rules were performed. No formal stopping rules were predetermined. Instead, the data and safety monitoring board evaluated the data and each serious adverse event and decided whether the trial should be continued.

To comply with Good Clinical Practice guidelines, a monitoring plan was made.[37] Data monitoring was performed in February 2013, and was repeated after enrollment ended in February 2014.

RESULTS

Figure 1 Flowchart of the study patients.



Abbreviations: CT; Computed Tomography, GSW; Gun Shot Wounds, cp resuscitation; cardiopulmonary resuscitation.

*3860 patients were excluded, but could have more than 1 reason to be excluded; therefore, the numbers do not total 3860.

Study population

Patient enrollment began on April 22, 2011, and ended on January 1, 2014 at 4 hospitals in the Netherlands and one hospital in Switzerland. According to the CONSORT statement, the number of patients involved in the trial from assessment of eligibility to analysis of the primary endpoint is shown in Figure 1. Of all the randomized patients, 203 were excluded after randomization (details are described in the Appendix, Table 4). In total, 541 patients were randomized to an immediate total-body CT scan and 542 patients to the standard workup group.

There were 6 crossovers (1.1%) in the TBCT group versus 18 (3.3%) in the standard workup group (P=0.21). Other protocol violations, not classified as crossovers by the Steering Committee, were found in 49 (9.1%) TBCT patients versus 62 (11.4%) of the standard workup patients (P=0.196). Details are described in the Appendix, Table 5.

Table 1 shows the baseline demographics and clinical characteristics of the included patients. The groups were comparable for all characteristics except for the number of polytrauma patients (TBCT versus standard workup) (362 [66.9%] vs. 331 [61.1%], P=0.045), hemoglobin level (129 vs. 133 g/dl, P=0.003) and hematocrit level (0.38 vs. 0.39 l/l, P=0.003). Median ISS (20 vs. 19, P=0.405) and the number of patients who received blood transfusions (147 [27%] vs. 150 [28%], P=0.867) were similar between groups. The distribution of ISS in 4 categories is shown in Figure 2.

Primary and secondary endpoints

Data on the primary and secondary endpoints are shown in Table 2. For the primary outcome of in-hospital mortality, no significant difference was found. Subgroup analyses of polytrauma patients and Traumatic Brain Injury (TBI) patients also revealed similar mortality rates between the two randomized cohorts.

Radiation exposure in the ED was increased in TBCT patients (20.9 mSv [IQR 20.6-20.9] vs. 20.6 mSv [IQR 9.9-22.1]), and was slightly increased during total hospital admission (21.0 mSv [IQR 20.9-25.2] vs. 20.6 mSv [11.8-27.6]). In the standard workup group, more patients were exposed to a lower radiation dose: 40% had a radiation dose that was below the lowest dose of patients who underwent a TBCT scan.

Table 1 Baseline demographic and clinical characteristics of the patients*

Characteristic	TBCT (nvs. Standard (n)†	Total-body CT (n=541)	Standard workup (n=542)
Age (years)	541 vs. 542	42 (27-59)	45 (26-59)
Male sex, n (%)	541 vs. 542	413 (76.3)	411 (75.8)
Blunt trauma, n (%)	541 vs. 542	530 (98.0)	533 (98.3)
Trauma mechanism blunt trauma, n (%)	530 vs. 534		
Fall from height		170 (32.1)	178 (33.3)
MVC – patient as occupant		201 (37.9)	190 (35.6)
MVC – patient as cyclist		65 (12.3)	60 (11.2)
MVC – patient as pedestrian		29 (5.5)	45 (8.4)
Other		65 (12.3)	61 (11.4)
Comorbidity, n (%)	517 vs. 521		
ASA I or II		495 (95.7)	501 (96.2)
ASA III, IV or V		22 (4.3)	20 (3.8)
Relevant medication, n (%)	505 vs. 516		
Coumarin derivatives		17 (3.4)	14 (2.7)
Thrombocyte aggregation inh.		38 (7.5)	28 (5.4)
Insulin		4 (0.8)	3 (0.6)
Pre-hospital vital parameters			
Respiratory rate (per minute)	323 vs. 317	17 (14-20)	16 (14-20)
Pulse (bpm‡)	470 vs. 478	90 (25)	88 (24)
Systolic BP (mmHg‡)	451 vs. 459	133 (31)	134 (31)
GCS (points)	528 vs. 533	14 (6-15)	14 (6-15)
Triage Revised Trauma Score	316 vs. 302	6.90 (5.03-7.84)	7.69 (5.03-7.84)
In-hospital vital parameters			
Respiratory rate (per minute)	330 vs. 339	16 (14-20)	16 (13-20)
Pulse (bpm‡)	528 vs. 531	88 (22)	87 (22)
Systolic BP (mmHg‡)	530 vs. 530	131 (26)	131 (29)
Hypotensive at admission, n (%)	-	38 (7.2)	44 (8.3)
GCS (points)	541 vs. 542	13 (3-15)	13 (3-15)
Revised Trauma Score	322 vs. 329	6.90 (4.09-7.84)	7.55 (4.09-7.84)
Laboratory results			
Hemoglobin level (g/dl)*	531 vs. 537	129 (113-142)	133 (120-145)
Hematocrit (l/l)*	478 vs. 488	0.38 (0.34-0.41)	0.39 (0.35-0.42)
pH	491 vs. 488	7.34 (7.28-7.38)	7.35 (7.29-7.39)
Base excess (mmol/l)	491 vs. 490	-2.1 (-4.7- -0.5)	-2.1 (-5.1- -0.1)
Abbreviated Injury Scale ≥3, n (%)	541 vs. 542		
Head		247 (45.7)	218 (40.2)
Chest		229 (42.3)	206 (38.0)
Abdomen		49 (9.1)	67 (12.4)
Extremities		150 (27.7)	154 (28.4)
Injury Severity Score (points)	541 vs. 542	20 (10-29)	19 (9-29)
Polytrauma patients, n (%)*§	541 vs. 542	362 (66.9)	331 (61.1)
TBI patients, n (%)§	541 vs. 542	178 (32.9)	151 (27.9)
TRISS, survival probability	317 vs. 301	0.93 (0.65-0.98)	0.94 (0.70-0.99)

*P>0.05 for all between-group comparisons except for hemoglobin level (P=0.003), hematocrit level (P=0.002) and polytrauma patients (P=0.045).
All data are number (%) or median (interquartile range) unless otherwise specified.
† This column displays the number of patients that was analyzed for each specific variable.
‡ Mean (SD).
§Polytrauma patients are defined as ISS ≥16. Traumatic Brain Injury (TBI) patients are defined as GCS <9 at presentation and AIS Head ≥3.
MVC denotes Motor Vehicle Collision, ASA denotes American Society of Anaesthesiologists, BP denotes Blood Pressure and TRISS denotes Trauma and Injury Severity Score.

Imaging time in the trauma room (30 min vs. 37 min, P<0.001) and time to diagnosis (50 min vs. 58 min, P<0.001) were decreased in TBCT patients. Time spent in the trauma room showed a trend towards less time spent at the ED for TBCT patients (63 minutes vs. 72 minutes, P=0.067).

The number of missed injuries found during the tertiary survey was similar in both groups (45 [8.8%] vs. 53 [10.1%], P=0.448).

The direct medical costs of the institutional stay were €24,967 (95% CI: €21,880– €28,752) for the TBCT group and €26,995 (95% CI: €23,326–€30,908) for the standard workup group (P=0.439).

Figure 2 Distribution of ISS between randomization groups

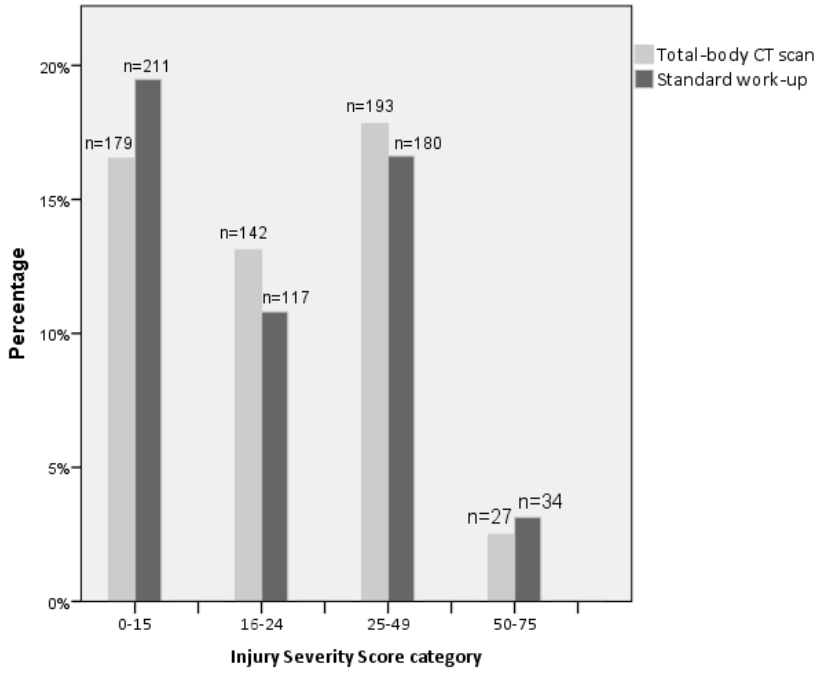


Table 2 Primary and secondary endpoints

Characteristic	TBCT (n) vs. Standard (n)	Total-body CT (n=541)	Standard workup (n=542)	P-value
Mortality				
In-hospital mortality, n (%)				
All patients, intention-to-treat§	541 vs. 542	86 (15.9)	85 (15.7)	0.923†
Polytrauma patients ‖	362 vs. 331	81 (22.4)	82 (24.8)	0.457†
Patients with severe TBI ‖	178 vs. 151	68 (38.2)	66 (43..7)	0.311†
24-hour mortality, n (%)				
All patients, intention-to-treat	541 vs. 542	43 (7.9)	33 (6.1)	0.231†
Polytrauma patients	362 vs. 331	41 (11.3)	33 (10.0)	0.564†
Patients with severe TBI	178 vs. 151	37 (20.8)	27 (17.9)	0.507†
Time intervals				
Time to end of imaging (minutes)				
All patients, intention-to-treat	429 vs. 424	30 (24-40)	37 (28-52)	<0.001*
Polytrauma patients	289 vs. 253	32 (24-41)	38 (29-53)	<0.001*
Patients with severe TBI	148 vs. 117	31 (23-41)	35 (27-47)	0.007*
Time to diagnosis (minutes)				
All patients, intention-to-treat	415 vs. 410	50 (38-68)	58 (42-78)	0.001*
Polytrauma patients	276 vs. 245	52 (40-69)	63 (45-81)	0.001*
Patients with severe TBI	141 vs. 114	49 (39-63)	54 (41-73)	0.070*
Time at ED (minutes)				
All patients, intention-to-treat	423 vs 416	63 (47-102)	72 (50-109)	0.067*
Polytrauma patients	285 vs. 252	69 (49-109)	82 (57-119)	0.011*
Patients with severe TBI	144 vs. 119	66 (49-95)	74 (52-114)	0.083*
Radiation exposure¶				
Trauma resuscitation room (mSv)				
All patients, intention-to-treat	520 vs. 531	20.9 (20.6-20.9)	20.6 (9.9-22.1)	<0.001*
Polytrauma patients	346 vs. 323	20.9 (20.1-20.9)	20.6 (17.6-22.7)	0.272*
Patients with severe TBI	172 vs. 146	20.9 (20.0-20.9)	20.6 (10.5-22.4)	0.040*
Total during hospital stay (mSv)				
All patients, intention-to-treat	520 vs. 531	21.0 (20.9-25.2)	20.6 (11.8-27.6)	<0.001*
Polytrauma patients	346 vs. 323	22.3 (20.7-26.5)	22.5 (20.0-33.1)	0.766*
Patients with severe TBI	172 vs. 146	22.7 (20.6-26.4)	21.4 (15.1-29.1)	0.068*
Direct medical costs - € (95% CI)	479 vs. 488	24,967 (21,880-28,752)	26,995 (23,326-30,908)	0.439
	541 vs. 540	129 (23.8)	124 (23.0)	0.732†
Complications, n (%)				
Transfusions in-hospital, n (%)**	540 vs. 542	148 (27.4)	150 (27.7)	0.907†
Length of stay (days††				
Total hospital stay	483 vs. 494	10 (4-20)	9 (3-19)	0.110*
ICU stay	286 vs. 295	3 (1-8)	3 (1-8)	0.825*
Ventilation days	286 vs. 295	2 (1-5)	1 (1-6)	0.779*
Tertiary survey				
Missed injuries found, n (%)**	541 vs. 542	45 (8.8)	53 (10.1)	0.448†
Serious Adverse Events, n (%)‡‡	541 vs. 542	3 (0.6%)	1 (0.2%)	0.374‡

Data are number (%) or median (interquartile range [IQR]) unless otherwise indicated.
TBI denotes Traumatic Brain Injury. ED denotes Emergency Department.
*Mann-Whitney U test; †Chi^2 test; ‡Fisher's Exact Test.
§ Outcome remained similar in all endpoints with a per-protocol analysis in which crossovers were excluded.
|| Subgroups were specified in advance. Polytrauma patients are patients with ISS ≥16. TBI was defined as an admission Glasgow Coma Scale (GCS) ≤8 and an Abbreviated Injury Score (AIS)-head of ≥3.
¶ Excluded are patients who died at the ED (6/1.1% TBCT patients vs. 4/0.7% standard workup patients) and patients with incomplete follow-up for radiation exposure (15/2.8% TBCT patients vs. 7/1.3% standard workup patients).
** Number of patients who received blood transfusions during hospital stay (i.e. packed cells, thrombocytes, plasma) and the number of patients for whom missed injuries were detected during the tertiary survey.
††Total hospital stay is unknown in case a patient is transferred to another hospital and date of discharge to own housing conditions could not be retrieved.
‡‡ One other SAE occurred in the post-randomisation patients. Details of the SAEs are described in the Appendix.

Per-protocol analysis

In the per-protocol analysis, 24 crossovers (i.e., patients who received the opposite intervention to which they had been allocated) were excluded. No significant differences in outcome were found for all endpoints.

Serious adverse events

Five serious adverse events (SAEs) were reported during the course of the trial. Three were reported in TBCT patients (0.6%) and one SAE occurred in the standard workup group (0.2%). One SAE was reported in a post-randomization excluded patient. Details of these SAEs can be found in the Appendix.

DISCUSSION

In this randomized multicenter trial, we found no significant difference in immediate total-body CT scanning compared with the standard workup with conventional imaging and selective CT scanning with respect to in-hospital mortality in severe trauma patients. The radiation dose was slightly increased in the TBCT patients, and substantially more patients in the standard workup group received a lower radiation dose. There is a time benefit for time to diagnosis and imaging time in the trauma room in favour of TBCT scanning. The number of missed injuries found during the tertiary survey and direct medical costs was similar in both groups.

During the last few years, several mostly retrospective studies showed an association between TBCT scanning and survival in trauma patients, as was summarized in 6 systematic reviews.[2,23-27] Huber-Wagner et al. repeatedly showed a decrease in absolute mortality rates and an increase in the probability of survival in polytrauma patients (ISS ≥16) who had received a total-body

CT scan (compared with non-TBCT) in a large cohort of patients from the German Trauma Registry.[3,13] The major difference between this study and the REACT-2 trial is that the study of Huber-Wagner and colleagues is retrospective. The authors had to use a risk-adjusted approach and multivariate analysis to adjust for possible confounders. As yet, there is no consensus on the appropriate selection criteria for patients eligible for a TBCT scan. In some centers, the trauma team leader decides whether to select a patient for total-body CT,[11,38] whereas in other centers the selection is based on a 3-tier structure with vital parameters, clinical suspicion of specific injuries and injury mechanisms, as was used in the present study.[5,39] As a consequence of our randomized design, we included a considerable number of patients with an ISS lower than 16 (35%). This reflects daily practice and the difficulties in preventing over- or undertriage, but possibly confounds the association between survival and total-body CT scanning. Although severely injured patients can be expected to benefit most from the rapid and detailed overview of the TBCT scan, the differences between the two randomized groups might be narrowed due to the relatively high number of patients with less severe injuries. Nevertheless, the subgroup analyses of polytrauma patients and traumatic brain injury patients also revealed no differences with regard to in-hospital mortality. Further refinement of appropriate selection criteria is a challenge for future studies.

The need to limit the amount of the radiation dose is another important factor in determining which patients might benefit from an immediate TBCT scan. CT scanning is associated with a high radiation dose, which could contribute to an increased lifetime cancer risk.[15] The present study shows that 40% of the patients in the standard workup group had a radiation dose below the lowest radiation dose of patients who underwent a TBCT scan. The substantial number of patients in the standard workup group having had a low radiation dose might have been due to having 35% non-polytrauma patients in our study population.

The time benefit with the use of TBCT has been shown previously.[28] This benefit is in line with the results of the present study, which showed a time benefit of 7 minutes in time to diagnosis in all patients, and a time benefit of 11 minutes in the polytrauma patients. Although a time benefit of 7 minutes might seem marginal, it is in fact relevant because it comprises 10% of the median time spent in the trauma room (69 minutes for all included patients). Nevertheless, all registered time intervals appear to be relatively long because a TBCT scan can technically be obtained in 5 minutes. Explanations might be that patient transfers, ATLS® primary surveys and life-saving interventions in the trauma room are time-consuming, particularly in severely injured patients, or that registered time intervals are lagging behind the real time intervals.

It must be noted that confidence in the safety of a TBCT scan is a concern of the complete multidisciplinary trauma team. We found a low number of SAEs during the course of the trial. Although all the SAEs occurred during CT scanning, a high risk of SAE was noted by the entire

trauma team in these specific cases. We hypothesized that in the case of severe injuries combined with increased age and a compromized medical history, with associated very low probability of survival, the trauma team sometimes accepts extra minutes of diagnostic time and proceeds with CT scanning to exclude salvageable injuries instead of performing potentially futile invasive procedures.

Limitations and strengths

The limitations of this study should be acknowledged. First, the results show that 250 (46%) of the patients in the standard workup group underwent sequential segmental CT scans of all body regions, comprising a TBCT scan in the end. This high percentage might introduce a bias in the interpretation of our results, given the differences between the groups with respect to mortality might be narrowed by the increased amount of non-immediate TBCT scans in the standard workup group. Although we discussed this phenomenon, we aimed to keep the study as close to daily practice as possible and therefore did not impose on the participating centers to change their local protocols for obtaining CT scans of specific body regions.

Second, the number of TBCT scans in the standard workup group might have been increased due to a learning curve experienced by trauma team members during the course of the trial. An alternative to the present study design with respect to imaging protocols would have been that all participating hospitals had to perform a specific imaging and contrast administration protocol in both study arms. However, there is no solid scientific basis for the choice and preference of one imaging protocol over another, and participating hospitals would have had to change their current practice. This requirement likely would have increased the risk of protocol violations. Also, the introduction of a new protocol is associated with the usual learning curve disadvantages. In addition, such a forced use of imaging protocols would ignore the wide variation in imaging protocols used worldwide, thereby limiting the external validity of the trial results.

Third, a certain degree of subjectivity could not be prevented with respect to the inclusion and exclusion criteria. For example, determining whether a trauma mechanism was high- or low-energetic is not a measurable criterion. Defining these criteria gives an appearance of objectivity (e.g., a high-energy trauma defined as "MVC with >50km/hr"), whereas in daily practice individual interpretations by witnesses or ambulance personnel will occur. Our pragmatic design has led to a considerable number of post-randomization exclusions because of inappropriate enrollment. We did find a wide variety in the amount of post-randomization exclusions between the participating sites (shown in the Appendix, Table 4), that might be explained by differences in experience with the use of a TBCT scan. Nevertheless, being too strict with regard to the inclusion criteria in an acute setting will lead to a higher rate of excluded patients who otherwise might have potentially benefitted from the TBCT scan.

Lastly, similar arguments are applicable to the number of protocol violations. More experience with the use of a TBCT scan might decrease the number of protocol violations. Protocol violations are not routinely described in previous studies, but that does not mean that they did not occur. The strength of the present study is the clear and detailed description of these violations, which were justified based on clinical grounds in 24% of the cases.

Considering strengths, this is the first international multicenter randomized study of immediate TBCT scanning in severe trauma patients with prospective clinically based inclusion criteria. Its overall design and randomization stratification protocol per hospital ensured that the randomized cohorts were equal in patient characteristics, treatment modalities and prior probability of survival. Furthermore, the pragmatic design described above will facilitate trial results being generalizable and thus applicable to the various trauma imaging settings worldwide. Finally, the detailed description of the study method, including the missing variables lacking in most studies, increases the chance of reproduction of the trial, which we would warmly encourage.

CONCLUSION

Total-body CT scanning is safe, shortens the time to end of imaging and does not increase direct medical costs; however, it does not improve survival. Also, many patients in the standard workup group received lower total radiation doses.

CONTRIBUTORS

All authors contributed to the study design, writing of the manuscript, and the decision to submit for publication. KT and JCS gathered and analyzed the data. MGD performed the cost-analysis. LFB contributed to the radiation dose calculation. JCS wrote the manuscript and created the figures under supervision of JCG. All authors contributed equally in editing the manuscript and accepted the manuscript in its present form.

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APPENDIX

Table 1 Inclusion and exclusion criteria

Inclusion criteria

Trauma patients with one of the following parameters at hospital arrival:

- respiratory rate ≥30/min or ≤10/min
- pulse ≥120/min
- systolic blood pressure ≤100 mmHg
- estimated exterior blood loss ≥500 ml
- Glasgow Coma Score ≤13
- abnormal pupillary reaction

OR

Patients with a clinical suspicion of one of the following diagnoses:

- fractures from at least two long bones
- flail chest, open chest or multiple rib fractures
- severe abdominal injury
- pelvic fracture
- unstable vertebral fractures / spinal cord compression

OR

Patients with one of the following injury mechanisms:

- fall from a height (>3 meters / >10 feet)
- ejection from a vehicle
- death of occupant in same vehicle
- severely injured patient in same vehicle
- wedged or trapped chest / abdomen

Exclusion criteria

Trauma patients with one of the following characteristics will be excluded:

- known age <18 years
- known pregnancy
- referred from another hospital
- clearly low-energy trauma with blunt injury mechanism
- any patient with a stab wound in one body region
- any patient who is judged to be too unstable to undergo a CT scan and requires (cardiopulmonary resuscitation or immediate operation because death is imminent)

APPENDIX

Table 2 Effective doses for single-pass computed tomography procedures in trauma.

Examination	Average effective dose (mSv)
Total-body	20.9*
Brain	1.8
Face	1.8
Sinuses	0.6
Mastoid	0.36
Cervical spine	3
Chest	5.1
Thoracic spine	12
Shoulder	1
Abdomen	11
Upper abdomen	6.5
Kidney	11
Lumbar spine	12
Pelvis	4.5

Abbreviations: CTA, Computed Tomography Angiography; mSv, millisievert. *Calculated as the sum of CT-brain, cervical spine, chest and abdomen.

APPENDIX

Table 3 Indications for Selective CT scanning after conventional imaging

CT-brain

A patient with trauma of the head and with at least:

1 major criterion:

- EMV ≤13
- loss of consciousness >30 minutes
- hemodynamically unstable
- age ≥60 years
- high-risk trauma
- vomiting
- posttraumatic seizure
- coagulopathy risk factors (primary or by medication)
- focal neurological deficit
- >1 point decline in EMV after 1 hour
- posttraumatic amnesia >4 hours
- clinical suspicion for skull base or facial fractures

and/or at least 2 minor criteria:

- age between 40-60 years
- posttraumatic loss of consciousness
- posttraumatic amnesia 2-4 hours
- externally facial injuries without signs of fractures
- 1 point decline in EMV after 1 hour

CT of the cervical spine

1. Always when CT-brain is performed
2. In all patients unless they meet all the Nexus criteria:

- no posterior midline cervical spine tenderness
- no focal neurological deficit
- a normal level of alertness
- no evidence of intoxication
- no painful distracting injuries

X-cervical spine

Never indicated. If Nexus deviant: cervical-CT.

Abdominal CT (with iv contrast)

1. Penetrating injuries in abdomen, chest and/or flank
2. Deficits found with FAST
   - intra-abdominal free fluid
   - suspicion organ injury
   - suspicion retroperitoneal injury
3. Dislocated pelvic ring fracture and/or dislocated acetabulum fracture
4. Clinical suspicion of intra-abdominal injury at physical examination
5. Subjective judgment of severity of injury by trauma leader
   - combined thoracic and pelvic injury
   - 'seatbelt sign'
   - chance fracture

X-thoracic and lumbar spine

Not indicated when chest or abdominal CT is performed (reconstructions can be made)

1. Complaints of the thoracic and lumbar spine
2. Tenderness of the thoracic and lumbar spine in the midline
3. Loss of consciousness
4. Deficits in peripheral neurologic examination
5. Painful distracting injuries

Pelvic CT (with iv contrast

1. All pelvic ring and acetabulum fractures unless conventional imaging is sufficient for adequate diagnosis and treatment
2. After reposition of hip luxation with suspicion of femoral head fractures and/or acetabulum fracture.

When CT-abdomen is performed, CT-pelvis is not necessary.

Table 3 *Continued*

Chest CT (with iv contrast) 1. Chest gunshot wound with suspicion of transmediastinal route 2. Acute aortic injury 3. Abnormal mediastinum seen at chest radiography. - mediastinal widening - pleural cap ('apical cap') - aorta arc unclear enclosed - left main bronchus removed downwards - deviated trachea or esophagus - filled aortopulmonary window - widened paraspinal line - widened paratracheal line right 4. Relative indications: - type and severity of trauma - fractures of costa 1 or 2 - thoracic spine fracture - posterior sternoclavicular luxation - hesitation about the existence of pneumothorax / pneumomediastinum or pneumopericardium - fractures of the clavicle and shoulder	**Retrograde urethrogram** 1. Male patient with severe pelvic injury (type B and C) 2. Bleeding from the meatus, perineal injury or injury of the outer genital organs 3. Penetrating abdominal injury 4. In women only selectively after inspection **Imaging of the extremities** When fractures/dislocations are suspected: conventional imaging and selective CT.

Appendix

Table 4 Post-randomization exclusions per center

	Center A n=354	Center B n=291	Center C n=363	Center D n=145	Center E n=133	Total n=1286
Randomized to Standard workup						
Known age <18 years			2			2
Known pregnancy						0
Referred from another hospital	1		2			3
Clearly low-energy trauma with blunt injury mechanism	9	26	12	5	3	55
Penetrating injury in one body region (except GSW)	1		1			2
Too unstable to undergo CT scan*			1	3	3	7
Second enrolment in trial		1	1			2
Does not fulfil inclusion criteria		14	8	2	5	29
Randomized to TBCT						
Known age <18 years			1			1
Known pregnancy						0
Referred from another hospital			1			1
Clearly low-energy trauma with blunt injury mechanism	17	13	17	5		52
Penetrating injury in one body region (except GSW)		2	1			3
Too unstable to undergo CT scan*	2	3	4	4	1	14
Second enrolment in trial	1					1
Does not fulfil inclusion criteria	2	10	8	6	5	31
Total	33 (9.3%)	69 (23.7%)	59 (16.3%)	25 (17.2%)	17 (12.8%)	203 (15.8%)

CT denotes Computed Tomography, GSW denotes gunshot wounds.

*Too unstable for CT scan ((cardiopulmonaryresuscitation or immediate operation is required because death is imminent).

Appendix

Table 5 Protocol violations

	Center A n=321	Center B n=222	Center C n=304	Center D n=120	Center E n=116	Total n=1083
Randomized to Standard workup						
No chest X-ray performed					1	1
No pelvic X-ray performed	4	5	5	1	11	26
No FAST performed		2	1	3		6
No chest and pelvic X-ray performed		3	4		4	11
No pelvic X-ray and FAST performed	2		3	5		10
TBCT after conventional imaging		1	2			3
Selective CT prior to standard workup		1			2	3
No spinal X-rays performed, spinal CT instead	1			1		2
Randomized to TBCT						
TBCT not completed	2		2	1		5
TBCT not completed + prior FAST					2	2
Chest X-ray performed before TBCT	3	2	2	1		8
Pelvic X-ray performed before TBCT		1				1
FAST performed before TBCT		3	6		1	10
Chest X-ray and FAST performed before TBCT		1	2			3
Chest and pelvic X-ray performed before TBCT	2	2	1	1		6
Chest and pelvic X-ray + FAST performed before TBCT		7	5	2		14
Total	**14 (4.4%)**	**28 (12.6%)**	**33 (10.9%)**	**15 (12.5%)**	**21 (18.1%)**	**111 (10.2%)**
Protocol crossovers		4	5	4	11	24
TBCT instead of standard workup		3	5	0	10	18
Standard workup instead of TBCT		1	0	4	1	6
Total protocol violations	14 (4.4%)	32 (14.4%)	38 (12.5%)	19 (15.8%)	32 (27.6%)	(12.5%)
Total protocol violations with unknown reasons*	11 (3.4%)	28 (12.6%)	19 (6.3%)	13 (10.8%)	32 (27.6%)	103 (9.5%)

*Total number of protocol violations when excluding patients for whom deviation of protocol had a clear clinical reason (e.g., transportation to OR or angiosuite)

Appendix. Serious Adverse Events (SAEs described in detail)

Patient A: An 81-year-old woman was randomized for immediate total-body CT. Because of respiratory and hemodynamic instability (blood pressure [BP] 80/40 mmHg, pulse [P] 80/min, Glasgow Coma Score [GCS] 3, on-scene endotracheal intubation) the randomization result was not followed and chest and pelvic X-rays and FAST were performed. A pneumothorax was seen on the chest x-ray and two chest tubes were placed. Before starting the CT brain the trauma team decided not to resuscitate in case of cardiac arrest. CT scanning was interrupted because of respiratory instability. The patient died shortly after.

Patient B: A 75-year-old man was randomized for immediate total-body CT. Because blood pressure and pulse were considered acceptable (BP 130/100 mmHg, P 110/min, GCS 3, on-scene endotracheal intubation), the trauma team decided to proceed with the CT scan. During the scanning, the clinical condition of the patient deteriorated and the scan was interrupted. Physical examination and ultrasound did not reveal a cardiac tamponade or tension pneumothorax. The patient died due to his traumatic injuries after a short period of cardiopulmonary resuscitation and insertion of a chest tube.

Patient C: A 74-year-old woman was randomized for immediate total-body CT. There was a discrepancy between the detection of carotid and femoral pulsations, but the vital parameters were considered acceptable (BP 128/95 mmHg, P 80/min, GCS 3, on-scene endotracheal intubation). Therefore, the trauma team decided to proceed with a CT scan to guide therapeutic interventions. When the total-body CT scan was almost finished, the patient developed severe bradycardia and the scan was interrupted. During cardiopulmonary resuscitation, the CT brain was evaluated and the traumatic brain injury was diagnosed as incompatible with life. The cardiopulmonary resuscitation was discontinued and the patient died.

Patient D: an 86-year-old woman was randomized for conventional imaging. Upon arrival at the Emergency Department the vital parameters were marginal (BP 94/52 mmHg, P 69/min, GCS 3, on-scene endotracheal intubation). Given her compromized medical history, the decision was made not to resuscitate in case of an event during scanning. After conventional imaging there was an indication for TBCT. During the scan there was no cardiac output. The patient died in the trauma room.

There was also 1 SAE reported in the post-randomization exclusions. This 86-year-old woman was randomized for immediate total-body CT, but should have been excluded. During the scanning, a massive pneumothorax was found and the scan was interrupted. Two chest tubes were inserted and shortly after this procedure the patient died, following a short period of cardiopulmonary resuscitation.

SUMMARY OF THE THESIS AND FUTURE PERSPECTIVES

SUMMARY OF THE THESIS

Computed tomography (CT) scanning has become essential in the early diagnostic phase of trauma care. It is a fast and highly accurate modality for the identification of various injuries and it enables a rapid response to life-threatening problems. Especially total-body CT (TBCT) scanning is increasingly used. The TBCT scan can be used as a supplement to conventional imaging (i.e. chest and pelvic x-rays, FAST and selective CT scanning), but also as a total replacement. The aim of this thesis was to clarify the role of (immediate) TBCT scanning in severely injured patients, considering its benefits and boundaries.

In **Chapter 1** a systematic review and meta-analysis on the significance of immediate TBCT scanning was described. The main outcomes were overall mortality and time spent in the emergency room (ER). After a systematic search of the literature, four studies were included describing a total of 5470 patients. All four studies were non-randomized retrospective cohort studies. Mortality was reported in three studies. Absolute mortality rates differed substantially between studies, but within studies mortality rates were comparable between immediate TBCT scanning and conventional imaging strategies. Time in the ER was described in three studies, and was significantly shorter in two studies in patients who underwent immediate TBCT (70 vs 104 minutes and 47 *vs* 82 minutes respectively). The substantial reduction in time in the ER is a promising feature of immediate TBCT scanning, but well designed and larger randomized studies are needed to see how this will translate into clinical outcomes.

In **Chapter 2**, we examined the reliability of time intervals recorded in an academic Level-1 hospital database during trauma survey. Time intervals (such as time spent at the trauma room, or time to intervention) are often mentioned in studies on the topic of TBCT scanning, and their reliability is therefore an important topic. Furthermore, time intervals are increasingly used as performance indicators. Dedicatedly recorded time intervals were compared with the routinely recorded data from February 2012 to June 2012. Dedicated time registration was done by an independent researcher who was not involved in actual trauma care. Time intervals that were done as a standard operational procedure (either fully computerized or by nursing staff), were retrieved from several hospital databases and were called 'routinely recorded'. In a convenience sample of 100 trauma patients dedicatedly registered median trauma room time was 47 minutes, compared to 42 minutes in routinely recorded in hospital databases ($P < 0.001$). Time to start of CT scanning differed significantly as well, with a larger dedicatedly registered time interval compared to the routinely recorded time registration. Bland-Altman plots showed wide 'limits of agreement', reflected by the small sample size and great variation of the differences. For example, the routinely recorded total trauma room time may be 45 minutes below or 57 minutes above the dedicatedly recorded time. Although most observations are within the limits of agreement, we assumed that the wideness of the limits would be relevant for research

purposes. For the time intervals trauma room to ICU and trauma room to intervention there were wide intervals, but those are difficult to interpret due to the small sample sizes. This study showed that routinely recorded time intervals in the trauma care setting might not be very reliable.

The study described in **Chapter 3** compared different scanning protocols in TBCT scanning regarding to the sequence and timing of intravenous contrast administration in three series of 10 consecutive trauma patients. A total-body CT scan comprises a scan from head to symphysis pubic (i.e. CT brain, cervical spine, chest and abdomen incuding the pelvis). Intravenous contrast is given to assure that bleeding sites can be identified. This study compared three different scanning protocols. In Group A unenhanced brain and cervical spine CT was followed by chest–abdomen-pelvis CT in portovenous phase after raising the arms beside the head. Group B underwent brain CT followed by a one-volume contrast CT from skull base to the pubic symphysis, without arm repositioning. Group C was identical to Group A, but the trunk was scanned with a split bolus technique. Three radiologists independently evaluated protocol quality scores (5 point Likert scale), parenchymal and vascular enhancement and artifacts. It was shown that in single-pass total body CT scanning a split bolus technique reached the highest overall image quality, compared to conventional TBCT and one-volume contrast CT.

In a retrospective case-matched series described in **Chapter 4**, it was shown that trauma patients who underwent immediate TBCT scanning (n=152) had similar crude 30-day mortality rates (13% in both groups, P=1.000) compared to patients who underwent conventional imaging supplemented by selective CT scanning (n=152). However, immediate TBCT scanning was associated with decreased 30-day mortality after correction for the impact of differences in Injury Severity Score (ISS) and in-hospital Glasgow Coma Score (GCS).

The study described in **Chapter 5** investigated incidental findings associated with immediate TBCT scanning. TBCT scanning was performed in 321 patients between 2009 and 2011. Incidental findings were divided in three categories: category I (potentially severe condition, further diagnostic work-up is required), category II (diagnostic work-up dependent on patients' symptoms and category III (findings of minor concern, no diagnostic work-up required). In 143 patients (44.5%), 186 incidental findings were reported. There were 13 category I findings (7%), 45 category II findings (24%) and 125 category III incidental findings (67%). Overall, 18 patients (5.6%) required additional diagnostic work-up. However, in 3 of these patients, there was no documentation of follow-up. In conclusion, the majority of incidental findings did not have clinical consequences. It was shown that documentation of incidental findings and their clinical consequences was incomplete and the findings of this study prompted us to add an item to our electronic trauma room report that obliges residents to report whether or not incidental findings are found during trauma imaging.

The difference in radiation dose before and after the introduction of a liberal policy towards TBCT scanning in polytrauma patients was determined in **Chapter 6**. Before the introduction of the TBCT scanning protocol (2008), 20% of the patients underwent a TBCT scan compared to 46% of the patients post-introduction of the TBCT scanning protocol (2010). Despite the increased amount of TBCT scans, the overall radiation dose during total hospital stay was comparable between patients in 2008 and 2010. This is most likely due to the fact that a TBCT scan during trauma survey provides more information than the conventional imaging strategy, thereby lowering the need for additional radiological imaging during hospital admission.

In **Chapter 7**, the REACT-2 study protocol is described. A previous trial, the REACT-1 trial, found that a CT scanner located in the trauma room reduces the time to acquire CT images and improves workflow, but does not lead to substantial improvements in clinical outcomes in a general trauma population. REACT stands for Randomized clinical trial of Early Assessment by CT scanning in trauma patients. The REACT-2 study aimed to determine the value of immediate TBCT scanning in trauma patients. It was an international, multicenter randomized clinical trial. All participating trauma centers had a multi-slice CT scanner located in the trauma room or at the Emergency Department (ED). Adult, non-pregnant, severely injured trauma patients according to predefined criteria were included. By randomization two groups were selected: the intervention group received a contrast-enhanced TBCT scan (head to pelvis) during the primary survey without prior conventional imaging. The control group was evaluated according to local conventional trauma imaging protocols consisting of X-rays and ultrasound (based on ATLS guidelines supplemented with selective CT scanning). Primary outcome was in-hospital mortality. Secondary outcomes included differences in mortality and morbidity during the first year post trauma, several trauma work-up time intervals, radiation exposure, general health and quality of life at 6 and 12 months post trauma and cost-effectiveness.

Finally, in **Chapter 8,** the results of the REACT-2 trial are described. In-hospital mortality rate was similar in the randomized groups (TBCT 15.9% vs standard 15.7%, P=0.923). Subgroups analyses in polytrauma patients (22.1% vs 24.8%) and Traumatic Brain Injury (TBI) (37.6% vs 43.7%) patients also showed similar in-hospital mortality rates between the randomized cohorts. Imaging time at the trauma room was decreased in the TBCT group (30 min vs 37 min, P<0.001). The limited absolute increase in median radiation dose during total hospital stay in the TBCT group masked the observation that substantially more patients in the standard work-up group received a lower radiation dose (21.0mSv (IQR=20.9-25.2) versus 20.6mSv (IQR=11.8-27.6), P<0.001). There were five serious adverse events (SAEs). Although four SAEs occurred during CT scanning, the high risk of a SAE was foreseen by the entire trauma team in advance in all these specific cases. The direct medical costs were €24,967 (95% CI: €21,880 – €28,752) for the TBCT group and €26,995 (95% CI: €23,326 - €30,908) for the standard work-up group (P=0.439). In conclusion, TBCT scanning was safe, shortened the time to end of imaging and

did not increase the medical costs, but it did not improve survival and many patients in the standard work-up eventually received lower radiation doses.

GENERAL CONCLUSION AND FUTURE PERSPECTIVES

Ongoing developments in the field of diagnostic imaging in trauma patients propose a major challenge to physicians. The TBCT scan provides a rapid and complete overview of possible life-threatening injuries that trauma patients can sustain, particularly internal bleeding. This total-body imaging concept is theoretically so promising that numerous trauma centers worldwide incorporated the TBCT scan in their daily practice, without Level 1 evidence. On the other side, TBCT scanning is associated with a considerable amount of radiation exposure and health care costs. Point of interest is whether it is safe to perform an immediate TBCT scan, with the omission of conventional imaging (X-rays and FAST). This thesis aimed to answer the question: will the advantages of a TBCT scan in trauma patients outweigh the disadvantages? The first randomized trial on this topic worldwide, the REACT-2 trial, partially provided us with answers: *No,* there is no difference in survival in trauma patients that undergo an immediate TBCT scan. *Yes,* 40% of the patients in the standard work-up had a radiation dose below the minimum radiation dose of patients who underwent a TBCT scan.
Yes, TBCT scanning is safe, shortens imaging time at the trauma room and does not increase the medical costs.

Future perspectives

Future studies should be directed to optimize the selection criteria for severely injured patients. The REACT-2 trial was one of the first trials that listed inclusion criteria to select severely injured (i.e. polytrauma patients) immediately after admission to the trauma room. Polytrauma patients are defined as patients with an Injury Severity Score (ISS) of 16 or above. In the REACT-2 trial, we aimed to include polytrauma patients solely, but in fact only 64% of the patients was severely injured. The study showed how difficult it is to determine which patients are severely injured on beforehand, as opposed to select polytrauma patients retrospectively, when results of radiography are known and an ISS is already attributed to the patient. The vital parameters, clinical suspicion of potential injuries and injury mechanisms used in the REACT-2 trial are a good, but certainly not the perfect starting point for future studies.

Theoretically, these less injured patients will benefit less from a TBCT scan. When the benefit decreases, disadvantages in terms of radiation dose and costs become more prominent. The REACT-2 showed that 40% of the patients in the standard work-up group had a radiation dose below the minimum radiation dose of patients who underwent a TBCT scan. Thus, if an individual patient is suspected to have a total radiation dose of 20 mSv or higher, this patient will have a lower radiation dose when evaluated with an immediate TBCT scan without previous

conventional imaging than when evaluated with the standard work-up. However, giving a proper estimation of the amount of radiation exposure a patient will receive, will be a challenge for a trauma team leader. Polytrauma patients, with multi-region injuries, are candidates for a higher radiation dose. Future studies should focus on how to identify these patients on beforehand, i.e. prior to diagnostic imaging. Until that time, the trauma team leader has to decide whether or not a TBCT scan is indicated in each individual trauma patient. Furthermore, improvements in scan algorithms may also help to further decrease the radiation dose.

Another point of interest is if the TBCT scan should be used as a supplement to or as a replacement of conventional imaging. In 9% of the REACT-2 patients randomized to an immediate TBCT scan, previous conventional imaging, such as a chest X-ray or FAST, was done. Whether this was strictly necessary, can be doubted. In our experience, the need for conventional imaging decreases with the increase of experience and confidence in the safety of the TBCT scan. Even in hemodynamically unstable patients, the TBCT scan can be a safe or even preferred imaging modality. If conventional imaging can be omitted, the radiation exposure in TBCT patients will further decline and more time will be saved. Since various level-1 trauma centers worldwide have already incorporated the use of the TBCT scan in their daily practice, it is unlikely that more randomized clinical trials on this topic will follow. However, prospective analysis of a cohort of hemodynamically unstable patients can provide information on the transition point between 'unstable but stable enough for a TBCT scan' and 'too unstable to perform a TBCT scan'. It has to be noted that close cooperation among the entire trauma team (trauma surgeons, anesthesiologists, radiologists) is essential to make an immediate TBCT scan possible. Also an optimal infrastructure and workflow are necessary to provide safe and rapid care to a trauma patient during the first diagnostic phase of trauma survey.

In Europe the CT scanner is located in or near the trauma room in almost all level-1 trauma centers and mostly used for blunt trauma patients. In North America however, penetrating injuries are more common and in this population, the role of total-body CT scanning is less clear. The REACT-2 study included only a small percentage of patients with penetrating injury and larger cohorts are needed to draw conclusions in this subgroup. Given the great variety in type and severity of penetrating injury (stab or gunshot wound, the presence or absence of an exit wound, the involvement of one or more body regions), an individual approach for each patient seems to be more suitable than performing a TBCT scan per se. For severe blunt trauma patients on the other hand, the REACT-2 trial shows that a TBCT scan is a safe and fast method, with similar costs involved compared to a standard radiological work-up. A CT scanner in or near the trauma room is therefore indispensable in a modern Level-1 trauma center, in both Europe and North America.

An interesting development is the integration of trauma resuscitation and management. The

hybrid operating room (OR), currently built in several trauma centers including the Academic Medical Center in Amsterdam, is a great example. In this multifunctional operating room, the trauma surgeon and the interventional radiologist can work together to provide an optimal form of care to the severely injured patient, following appropriate selection of patients by a TBCT in the trauma room. It is well possible that this room will be used as both a resuscitation room and operating room in the near future. Diagnostic procedures and management by surgeon or interventional radiologist can go hand in hand, in order to save time and provide the best care possible to the injured patient.

With these advancements in technology, cooperation between different trauma centers is of major importance to provide a clear and practical protocol for radiological imaging in severely injured patients. The continuation of joint scientific research is indispensable to draw useful conclusions.

NEDERLANDSE SAMENVATTING EN TOEKOMSTPERSPECTIEVEN

SAMENVATTING

De Computer Tomographie (CT) scan is cruciaal geworden in de vroege diagnostische fase van traumazorg. Het scannen zelf kan snel worden verricht met een hoge accuratesse voor het detecteren van veel verschillende letsels. Hierdoor is een snelle behandeling van levensbedreigende aandoeningen mogelijk. Recent is er steeds meer aandacht gekomen voor het scannen van het gehele lichaam (total-body CT scanning). Dit wordt dan vergeleken met de conventionele beeldvormingsstrategie die bestaat uit Röntgenfoto's, een echo van de buik en een CT scan van een specifiek lichaamsdeel op indicatie. De total-body CT scan kan aansluitend aan conventionele beeldvorming verricht worden, maar ook als vervanging van de conventionele beeldvorming dienen. Het doel van dit proefschrift was het verhelderen van de rol van de (directe) total-body CT scan bij de opvang van ernstig gewonde patiënten.

In **hoofdstuk 1** wordt een systematisch overzicht van de literatuur gegeven over de waarde van total-body CT scanning. De belangrijkste uitkomstmaten waren mortaliteit en totale tijd op de traumakamer. Na een systematische zoektocht in elektronische databases werden vier studies geïncludeerd die gezamenlijk een totaal van 5470 patiënten beschreven. Alle vier de studies waren niet-gerandomiseerde cohort studies met retrospectieve data collectie. Mortaliteit werd gerapporteerd in 3 studies. Absolute mortaliteitsaantallen verschilden substantieel tussen de studies, maar binnen studies waren de mortaliteitsaantallen vergelijkbaar tussen directe total-body CT scanning en de conventionele beeldvormingsstrategie. Tijd op de traumakamer werd beschreven in 3 studies, waarbij 2 studies lieten zien dat deze tijd significant korter was bij patiënten die een directe total-body CT scan kregen. De substantiële vermindering in tijd op de traumakamer als een directe total-body CT scan wordt gebruikt, is veelbelovend, maar er zijn beter opgezette en grotere studies nodig om te kunnen bepalen hoe zich dit laat vertalen naar klinische uitkomsten.

In **hoofdstuk 2** wordt de betrouwbaarheid beschreven van tijdsintervallen tijdens de trauma opvang zoals deze bijgehouden worden in de database van een academisch ziekenhuis (Level-1 trauma centrum). Tijdsintervallen (zoals totale tijd op de traumakamer of tijd tot interventie) worden vaak genoemd in studies naar het gebruik van een total-body CT scan en daarom is de betrouwbaarheid van deze tijdsintervallen relevant. Daarnaast worden tijdsintervallen in toenemende mate gebruikt als kwaliteitsindicatoren. Prospectief bijgehouden tijdsintervallen werden vergeleken met de automatisch bijgehouden tijdsintervallen tussen februari en juni 2012. De prospectieve tijdsintervallen werden bijgehouden door een onafhankelijke onderzoeker die niet betrokken was bij de trauma-opvang. De automatisch bijgehouden tijdsintervallen worden bijgehouden als standaard procedure (ofwel volledig geautomatiseerd ofwel door verplegend personeel) en werden verkregen uit ziekenhuis databases. In een groep van 100 patiënten was de prospectief bijgehouden tijd op de traumakamer mediaan 47 minuten, vergeleken met 42

minuten in de automatisch bijgehouden database (P < 0.001). Tijd tot start scannen was ook significant verschillend, met opnieuw een groter tijdsinterval bij de prospectief bijgehouden tijden vergeleken met de automatisch bijgehouden database. Nadere analyse van de data liet zien dat er een grote spreiding was in de resultaten, hetgeen in de praktijk betekende dat de automatisch bijgehouden tijdsintervallen 45 minuten onder of 57 minuten boven de prospectief bijgehouden tijden kon liggen. Ondanks dat de meeste observaties binnen deze 'limits of agreement' vielen, concludeerden we dat deze spreiding zeker relevant is als het gaat om de bruikbaarheid van deze getallen voor onderzoek. Voor wat betreft de tijdsintervallen van traumakamer naar de Intensive Care Unit (ICU) en van traumakamer tot interventie (bijv. operatie of embolisatie) golden eveneens zeer wijde intervallen, maar conclusies worden achterwege gelaten vanwege kleine aantallen. Deze studie liet zien dat automatisch bijgehouden tijdsintervallen niet zo betrouwbaar zijn als wordt gedacht.

De studie in **hoofdstuk 3** vergelijkt drie verschillende scanprotocollen die gebruikt kunnen worden bij het maken van een total-body CT scan in drie series van 10 trauma patiënten. Met een total-body CT scan wordt bedoeld een scan van kruin tot onderrand bekken (CT brein, cervicale wervelkolom, thorax en abdomen, inclusief bekken). Tijdens het scannen kan intraveneus contrast toegediend worden om bloedingen aan organen of vaten beter zichtbaar te maken. De drie series patiënten die vergeleken werden in dit hoofdstuk, werden gescand met drie verschillende scanprotocollen. In Group A werd een CT scan verricht van brein en de cervicale wervelkolom (CWK), gevolgd door een CT scan van thorax, abdomen en bekken in de portoveneuze fase nadat de armen boven het hoofd geplaatst zijn. In Group B werd de total-body CT scan in één keer uitgevoerd, zonder het verplaatsen van de armen. Group C was identiek aan groep A, met als verschil dat thorax en abdomen gescand werden met de zogenaamde 'split-bolus' techniek, waarin zowel de arteriële als de veneuze fase zichtbaar worden gemaakt. Dit laatste scanprotocol gaf de beste beeldkwaliteit.

In een retrospectieve serie die beschreven wordt in **hoofdstuk 4**, werd aangetoond dat trauma patiënten die een directe total-body CT scan ondergaan een vergelijkbare 30-dagen mortaliteit hadden in vergelijking met patiënten die geanalyseerd werden met de conventionele beeldvormingsstrategie. Wanneer gecorrigeerd werd voor factoren die de ernst van het trauma aangeven (zoals de Injury Severity Score en de Glasgow Coma Score), bleek een direct total-body CT scan wel geassocieerd met een lagere mortaliteit.

In **hoofdstuk 5** worden 'toevalsbevindingen' (een bevinding die niet gerelateerd is aan eventueel gevonden traumatische afwijkingen) als gevolg van een directe total-body CT scan beschreven. Tussen 2009 en 2011 kregen 321 patiënten een directe total-body CT scan. Toevalsbevindingen werden ingedeeld in 3 categorieën: categorie I (potentieel ernstige aandoening, verdere diagnostiek is nodig), categorie II (diagnostiek alleen indien aandoening symptomatisch is) en

categorie III (aandoening niet klinisch relevant, geen diagnostiek nodig). In totaal werden er bij 143 patiënten (45%), 186 toevalsbevindingen gevonden. Er waren 13 categorie I bevindingen (7%), 45 categorie II bevindingen (24%) en 123 categorie III bevindingen (67%). In totaal was er bij 18 patiënten (5.6%) additionele follow-up nodig. Bij drie van deze 18 patiënten was echter geen documentatie van follow-up. Concluderend bleek uit deze studie dat de meerderheid van de gevonden toevalsbevindingen geen follow-up behoefde. Daarnaast liet de studie zien dat de documentatie van toevalsbevindingen en hun klinische consequenties incompleet was. Als gevolg van deze studie werd een extra item toegevoegd aan het bestaande elektronische dossier, waardoor arts-assistenten die een trauma-opvang doen verplicht worden te rapporteren of er sprake is van toevalsbevindingen tijdens trauma-opvang.

Het verschil in stralingsdosis voor en na de introductie van een laagdrempelig protocol voor total-body CT scanning bij trauma patiënten wordt beschreven in **hoofdstuk 6**. Voor de introductie van dit protocol (2008) onderging 20% van de patiënten een total-body CT scan vergeleken met 46% van de patiënten na de introductie van dit protocol (2010). Ondanks de verdubbeling van het aantal total-body CT scans en de daarmee gepaard gaande hogere stralingsdosis op de traumakamer zelf, bleek dat de totale stralingsdosis tijdens ziekenhuisopname vergelijkbaar was tussen patiënten in 2008 en 2010. Hoewel niet onderzocht, is dit meest waarschijnlijk een gevolg van het feit dat een total-body CT scan op de traumakamer zoveel informatie oplevert, dat gedurende ziekenhuisopname minder radiologische onderzoeken worden verricht dan wanneer patiënt op de traumakamer de conventionele beeldvormingsstrategie ondergaat.

In **hoofdstuk 7** wordt het REACT-2 studieprotocol beschreven. De REACT-2 studie is een vervolg op de REACT studie waarin gevonden werd dat een CT scan gelokaliseerd op de traumakamer zelf in plaats van op de afdeling radiologie, de tijd tot scannen vermindert en daarmee het opvang-algoritme verbetert. REACT staat voor 'Randomized clinical trial of Early Assessment by CT scanning in trauma patients'. Er werd niet aangetoond dat dit de klinische uitkomst van de patiënt verbeterde. De REACT-2 studie had als doel het bepalen van de waarde van een directe total-body CT scan bij trauma patiënten. De studie is een internationale, multicentrische, gerandomiseerde klinische studie. Alle deelnemende centra hadden een CT scanner op de traumakamer zelf of op de spoedeisende hulp in de buurt van de traumakamer. Volwassen, niet zwangere, ernstig gewonde trauma patiënten werden aan de hand van vooraf vastgestelde criteria geïncludeerd. Door middel van randomisatie werden twee groepen gecreëerd. De interventiegroep kreeg een directe total-body CT scan (van kruin tot en met onderrand van het bekken) met intraveneus contrast. In de controlegroep vond diagnostiek plaats volgens de lokaal geldende conventionele beeldvormingsstrategie bestaande uit Röntgenfoto's, een echo van de buik en alleen op indicatie een CT scan van één of meerdere lichaamsdelen. Primaire uitkomst van de studie was ziekenhuis-mortaliteit. Secundaire uitkomstmaten waren verschillen in mortaliteit en morbiditeit tijdens het eerste jaar na het trauma, bepaalde tijdsintervallen tijdens

trauma-opvang, de hoeveelheid radiologische straling, algemene gezondheid en kwaliteit van leven na 6 en 12 maanden. Verder werd een kosten-effectiviteitsanalyse verricht.

Tenslotte worden in **hoofdstuk 8** de resultaten van de REACT-2 studie beschreven. In totaal werden 541 patienten geanalyseerd in de total-body CT groep en 542 patienten in de standaard work-up group (conventionele beeldvorming en een selectieve CT scan). Absolute mortaliteitscijfers waren vergelijkbaar (TBCT 15.9% versus standaard 15.7%, P=0.923). Subanalyses in multitrauma patiënten (22.1% versus 24.8%) en patiënten met ernstig hersenletsel (37.6% versus 43.7%) lieten ook vergelijkbare mortaliteitsaantallen zien tussen de gerandomiseerde groepen. Tijd van binnenkomst tot einde van de radiologische beeldvorming was korter in de total-body CT groep (30 minuten versus 37 minuten, P<0.001). Ondanks een kleine verhoging in stralingsdosis tijdens ziekenhuisopname op groepsniveau in de total-body CT groep (21.0 milliSievert (IQR=20.9-25.2) versus 20.6 milliSievert (IQR=11.8-27.6)), was er een substantieel aantal patienten in de standaard groep met een lagere stralingsdosis. De total-body CT scan was veilig om uit te voeren. Directe medische kosten waren vergelijkbaar in beide groepen (€24.967 versus €26.995, P=0.439).

ALGEMENE CONCLUSIE EN TOEKOMSTPERSPECTIEVEN

Ontwikkelingen op het gebied van radiologische beeldvorming bij trauma patiënten stellen clinici voor een grote uitdaging. De total-body CT scan geeft een snel en compleet overzicht van levensbedreigende letsels die een trauma patiënt kan hebben, in het bijzonder bloedingen. Deze scan is theoretisch zo veelbelovend, dat vele trauma centra de total-body CT scan al gebruiken bij de opvang van trauma patiënten, ook al is er nog niet voldoende betrouwbaar wetenschappelijk bewijs. Aan de andere kant is de total-body CT scan geassocieerd met een aanzienlijke hoeveelheid straling en zorgkosten. Deze thesis had tot doel het beantwoorden van de vraag: wegen de voordelen van een directe total-body CT scan, zonder voorafgaande conventionele beeldvorming, bij trauma patiënten op tegen de nadelen? De eerste gerandomiseerde klinische studie naar dit onderwerp wereldwijd, de REACT-2 studie, heeft ons deels van antwoorden voorzien.

Nee, er is geen overlevingswinst voor trauma patiënten die een directe total-body CT ondergaan.

Ja, er zijn aanzienlijk meer patienten met een lagere stralingsdosis in de standaard work-up groep.

Ja, de directe medische kosten zijn gelijk, er is tijdswinst bij het gebruik van de total-body CT scan en de directe total-body CT scan is veilig om uit te voeren.

Toekomstperspectieven

Toekomstige studies zouden zich moeten richten op het optimaliseren van de criteria voor het selecteren van ernstig gewonde patiënten. De REACT-2 studie was één van de eerste studies die criteria opstelde voor het selecteren van ernstig gewonde patiënten (multitrauma patiënten) direct na binnenkomst op de traumakamer. Het doel was om in de REACT-2 slechts multitrauma patienten te includeren, maar in de praktijk was 35% van de patienten minder ernstig gewond (dat wil zeggen: een Injury Severity Score (ISS) van lager dan 16). De studie liet zien hoe moeilijk het is om direct na binnenkomst op de traumakamer te bepalen of een patient ernstig gewond is, in tegenstelling tot het retrospectief selecteren van deze patiëntengroep wanneer de resultaten van radiologische beeldvorming bekend zijn en een ISS al is toegekend. De vitale parameters, klinische verdenkingen op letsels en specifieke ongevalsmechanismen zoals die gebruikt zijn in de REACT-2 studie zijn een goed, maar zeker niet perfect, startpunt voor toekomstige studies.

Theoretisch zullen minder ernstig gewonde patiënten ook minder profiteren van de voordelen van een total-body CT scan. Juist wanneer de voordelen afnemen, worden de nadelen in de vorm van stralingsdosis en zorgkosten meer prominent. De REACT-2 studie liet zien dat, ondanks een vrijwel gelijke mediane stralingdosis in beide groepen, een aanzienlijk deel van de patienten in de standaard work-up groep een lagere stralingsdosis kregen dan in de total-body CT groep. Desalniettemin was er ook een aantal patienten die juist een hogere stralingsdosis kregen in de standaard work-up groep, en juist deze patienten zouden voordeel hebben gehad van de total-body CT scan met het oog op de stralingsdosis. Hiermee wordt de noodzaak voor het opstellen van passende selectiecriteria onderstreept. De focus van toekomstige studies zou moeten liggen op het selecteren van criteria die voorspellend zijn voor ernstig letsel. Tot die tijd zal de traumateam leider voor elke individuele patient moeten beslissen of een total-body CT scan geïndiceerd is of niet.

Een ander punt van aandacht is of de total-body CT scan gebruikt zou moeten worden als toevoeging aan conventionele beeldvorming of als een vervanging hiervan. Bij 9% van de patienten in de REACT-2 studie die gerandomiseerd werden tot een directe total-body CT scan, is toch eerst conventionele beeldvorming gedaan (zoals een Röntgenfoto's van de thorax of een echo van het abdomen). Men kan zich afvragen of dit strikt noodzakelijk was. De ervaring leert dat de noodzaak voor conventionele beeldvorming voorafgaand aan een total-body CT scan afneemt wanneer de ervaring met en het vertrouwen in het gebruik van een total-body CT scan toeneemt. Ook bij hemodynamisch instabiele patienten kan de total-body CT scan veilig plaatsvinden of zelfs de voorkeur hebben. Als conventionele beeldvorming overgeslagen wordt, kan de stralingsdosis in de total-body CT groep verder worden verkleind en kan er meer tijd worden bespaard. Veel level-1 traumacentra gebruiken de total-body CT scan in hun dagelijkse trauma praktijk, daarom is het onwaarschijnlijk dat nog meer gerandomiseerde klinische studies naar dit onderwerp zullen volgen. Desalniettemin zijn grotere prospectieve series van

hemodynamisch instabiele patienten nodig om informatie te verkrijgen over waar de transitie ligt van 'instabiel, maar stabiel genoeg voor een total-body CT scan' naar 'te instabiel voor een total-body CT scan'.

Tegenwoordig is de CT scanner in vrijwel alle traumacentra in Europa gelokaliseerd op de traumakamer of daar dichtbij en is het gebruik ervan niet meer weg te denken uit de klinische praktijk. In Noord Amerika komen scherpe letsels meer voor dan in de meeste Europese traumacentra en in deze groep is het minder duidelijk wat de voorkeursmodaliteit van radiologische beeldvorming is. De REACT-2 studie heeft slechts een klein percentage patienten met scherpe letsels geincludeerd en grotere cohorten moeten worden onderzocht om zinvolle conclusies te kunnen trekken. De grote variatie in type en ernst van scherpe letsels (steek- of schotwond, aan- of afwezigheid van een uitschotopening en de betrokkenheid van één of meerdere lichaamsregio's) in het oog genomen, lijkt een individuele aanpak voor elke patient meer op zijn plaats dan een directe total-body CT scan. Voor stompe letsels daarentegen, laat de REACT-2 studie zien dat het verrichten van een directe total-body CT scan veilig en snel is, met vergelijkbare kosten vergeleken met een standaard radiologische work-up. Een CT scan in of vlakbij de traumakamer is daarom niet meer weg te denken uit een modern ziekenhuis, zowel in Europa als in Noord Amerika.

Een interessante ontwikkeling is de integratie tussen trauma-opvang en behandeling. De hybride operatiekamer, die momenteel gebouwd wordt in verschillende traumacentra waaronder het Academisch Medisch Centrum in Amsterdam, is daar een goed voorbeeld van. In deze multifuntionele operatiekamer, kunnen de chirurg en interventieradioloog samenwerken om de optimale zorg te leveren aan de ernstig gewonde trauma patiënten, nadat de juiste patienten hiervoor geselecteerd zijn middels een total-body CT scan. Mogelijk zal deze kamer in de toekomst gebruikt worden als kamer waar de traumapatiënt zowel opgevangen als behandeld kan worden. Zo kunnen diagnostiek en behandeling hand in gaan gaan waardoor tijd bespaard wordt en de beste zorg geleverd kan worden.

Met deze technologische vooruitgang is het van groot belang dat traumacentra samenwerken om te komen tot een duidelijk en praktisch protocol voor radiologische beeldvorming bij ernstig gewonde traumapatienten. Het voortzetten van gezamenlijk wetenschappelijk onderzoek is onontbeerlijk om waardevolle conclusies voor de dagelijkse praktijk te trekken.

PHD PORTFOLIO

Name PhD student:	J.C. Sierink
PhD period:	Oct 2010 – April 2013
Name PhD supervisor:	Prof. dr. J.C. Goslings

1. PhD training

	Year	Workload (Hours/ECTS)
General courses		
- Practical Biostatistics	2011	1.1
- Clinical data Management	2011	0.3
- BROK ('Basiscursus Regelgeving Klinisch Onderzoek')	2011	0.9
- Scientific writing in English for Publication	2011	1.5
- Project Management	2011	0.6
- Oral presentation in English	2011	0.8
Specific courses		
- Advanced Biostatistics	2013	2.1
Seminars, workshops and master classes		
- Weekly department seminars	2010-2012	3
- Master class by Prof. J. Powell	2012	0.2
Presentations		
Oral and posters		
- Systematic review and meta-analysis of immediate total-body computed tomography compared with selective radiological imaging of injured patients, *Ass. Symposium Traumachirurgie (Soestduinen), ECTES - poster (Milan, Italy)*	2011	1.0
- Use of flexion-extension cervical spine radiography in a level-1 trauma center, *ECTES - poster (Basel, Switzerland)*	2011	0.5
- Mythbuster: it is safe to omit routine repeat Hb measurement in hemodynamically stable trauma patients? *ECTES - poster (Lyon, France)*	2011	0.5
- A case-matched series of immediate total-body CT scanning versus the standard radiological work-up in injured patients, *Chirurgendagen (Veldhoven), ECTES (Basel, Switzerland), ECR (Vienna, Austria, presented by LFM Beenen)*	2012	1.5
- Automatically recorded versus prospective time registrations in the acute trauma care setting, *ECTES (Lyon, France, presented by EW de Jong)*	2013	0.5
- Time to intervention in patients with blunt splenic injury in a Dutch level 1 trauma center, *ECTES (Lyon, France, presented by DC Olthof)*	2013	0.5
- Multitrauma: to scan or not to scan? *Reünistendag Chirurgie AMC (Amsterdam).*	2014	0.5

(Inter)national conferences		
- NVT, *Amsterdam*	2010	0.25
- Ass. symposium traumachirurgie, *Soestduinen*	2011	0.25
- Chirurgendagen, *Veldhoven*	2011	0.25
- ESTES, *Milaan*	2011	0.25
- NVT, *Amsterdam*	2011	0.25
- Ass. symposium traumachirurgie, *Soestduinen*	2012	0.25
- Chirurgendagen, *Veldhoven*	2012	0.25
- ESTES, *Basel*	2012	0.25
- NVT, *Amsterdam*	2012	0.25
- Chirurgendagen, *Veldhoven*	2014	0.25

2. Teaching		
	Year	Workload (Hours/ECTS)
Teaching/supervising medical students/research nurses		
- M. Russchen, A case-matched series of immediate total-body CT scanning versus the standard radiological work-up in injured patients, Department of Surgery	2011-2012	2
- W. van Lieshout, Systematic review of the use of flexion-extension radiography of the cervical spine in symptomatic trauma patients, Department of Surgery	2011-2012	2
- G. Clerx, research nurse REACT-2 trial	2011-2013	2
- E. de Jong, Retrospective versus prospective time registrations in the acute trauma care setting, Department of Surgery	2012	2
- M. Wirtz, Radiation exposure before and after the introduction of a liberal policy towards total-body CT scanning in multi trauma patients, Department of Surgery	2013	2

3. Parameters of esteem	Year
Grants	
- ZonMW Doelmatigheids onderzoek	2010
- Stichting Prof. Boerema reisfonds	2014
Awards and Prizes	
Nominated for best poster at ECTES, Mythbuster: it is safe to omit routine repeat Hb measurement in hemodynamically stable trauma patients?	2013

LIST OF PUBLICATIONS

THIS THESIS

Sierink JC, Saltzherr TP, Beenen LFM, Luitse JSK, Hollmann MW, Reitsma JB, Edwards MJ, Patka P, Beuker BJA, Suliburk JW, Hohmann J, Dijkgraaf MGW, Goslings JC; the REACT-2 study group. **A multicenter, randomized controlled trial of immediate total-body CT scanning in trauma patients (REACT-2).** BMC Emergency Medicine 2012.

Sierink JC, Saltzherr TP, Reitsma JB, Van Delden OM, Luitse JSK, Goslings JC. **Systematic review and meta-analysis of immediate total-body computed tomography compared with selective radiological imaging of injured patients.** British Journal of Surgery 2012.

Sierink JC, Saltzherr TP, Beenen LFM, Russchen MJAM, Luitse JSK, Dijkgraaf MGW, J.C. Goslings JC. **A case-matched series of immediate total-body CT scanning versus the standard radiological work-up in injured patients.** World Journal of Surgery 2013.

Sierink JC, De Jong EW, Schep NWL, Goslings JC. **Routinely recorded versus dedicated time registrations during trauma work-up.** Journal of Trauma Management and Outcomes 2014.

Sierink JC, Saltzherr TP, Russchen MJAM, De Castro SMM, Beenen LFM, Schep NWL, Goslings JC. **Incidental findings on total-body CT scans in trauma patients.** Injury 2013.

Syrian JC, Saltzherr TP, Wirtz MR, Streekstra GJ, Beenen LFM, Goslings JC. **Radiation exposure before and after the introduction of a dedicated total-body CT protocol in multi trauma patients.** Emergency Radiology 2013.

Beenen LFM, Sierink JC, Kolkman S, Yung Nio C, Saltzherr TP, Dijkgraaf MGW, Goslings JC. **Split bolus technique in polytrauma: a prospective study on scan protocols for trauma analysis.** Acta Radiologica 2014.

Sierink JC, Treskes K, Edwards MJR, Beuker BJA, Den Hartog D, Hohmann J, Dijkgraaf MGW, Luitse JSK, Beenen LFM, Hollmann MW, Goslings JC; the REACT-2 study group. **Immediate total-body CT scanning versus conventional imaging and selective CT scanning in severe trauma patients: A randomized controlled trial (REACT-2 trial).** Submitted.

OTHERS

Sierink JC, Saltzherr TP, Edwards MJ, Beuker BJ, Patka P, Goslings JC, namens de REACT-2 studiegroep. **Directe total-body CT bij multitrauma patiënten – vooraankondiging lopend onderzoek.** Ned Tijdschr Geneeskd. 2012.

Sierink JC, Saltzherr TP, Beenen LFM, Luitse JSK, Hollmann MW, Reitsma JB, Edwards MJR, Patka P, Beuker BJA, Suliburk JW, Hohmann J, Dijkgraaf MGW, Goslings JC, the REACT-2 study group. **A randomized, controlled trial of immediate total-body CT scanning in trauma patients – letter to the Editor.** Emergency Medicine Australasia 2012.

Sierink JC, Schep NWL, Terra MP, Luitse JSK, Goslings JC. **A Case of Sequester and Involucrum Formation of the Fibula.**
J Med Cases 2012.

Sierink JC, Van Lieshout WAM, Beenen LFM, Schep NWL, Vandertop WP, Goslings JC. **Systematic review of flexion-extension radiography of the cervical spine in trauma patients.** Journal of European Radiology 2013.

Olthof DC, Sierink JC, van Delden OM, Luitse JSK, Goslings JC. **Time to intervention in patients with blunt splenic injury in a Dutch level 1 trauma center.** Injury 2013.

Sierink JC, Joosse P, De Castro SMM, Schep NWL, Goslings JC. **Does repeat Hb measurement within 2 hours after a normal initial Hb in stable trauma patients add value to trauma evaluation?** International Journal of Emergency Medicine 2014.

Sierink JC, De Castro SMM, Russell NS, Geenen MM, Steller EPh, Vrouenraets BC. **Treatment strategies in elderly breast cancer patients: is there a need for surgery?** The Breast 2014.

Sierink JC, Goslings JC. **A case-matched series of total-body CT scanning in trauma patients – letter to the Editor.** World Journal of Surgery 2014.

DANKWOORD

Wat mooi om nu, in navolging van mijn vader, te kunnen zeggen: 'Het is geklaard!'. Dit was niet gelukt zonder de hulp van velen. Ik wil graag een aantal mensen persoonlijk bedanken, maar mijn grootste dank gaat uit naar de patiënten die dit onderzoek mogelijk hebben gemaakt.

Mijn promotor Prof. J.C. Goslings, beste Carel. Jouw gedrevenheid en snelheid zijn ongekend. Het lijkt erop dat jouw dag meer dan 24 uur heeft. Stukken komen zonder uitzondering binnen enkele dagen terug, minutieus nagekeken met de rode pen. Ik heb veel bewondering voor de manier waarop jij je werk doet, als chirurg en wetenschapper, maar ook als persoon. Dank voor je vertrouwen en steun.

Mijn promotor Prof. M. Edwards, beste Michael. Onze eerste ontmoeting in het UMC Sint Radboud herinner ik me nog goed. De REACT-2 al in de steigers, maar de details over hoe de samenwerking moest verlopen nog niet rond. Onze felle discussie bleek garant te staan voor een vruchtbare samenwerking. Jouw betrokkenheid en passie voor onderzoek, met nadruk op toepasbaarheid in de praktijk, is van grote waarde geweest voor de REACT-2 studie en de totstandkoming van mijn proefschrift. Dank daarvoor.

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ABOUT THE AUTHOR

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Joanne Sierink werd geboren op 24 december 1983 in Assen. Het Gymnasium diploma behaalde zij aan CS Vincent van Gogh te Assen. Na twee jaar Psychologie gestudeerd te hebben aan Rijksuniversiteit Groningen, begon zij in 2004 met haar studie Geneeskunde aan dezelfde universiteit. Haar coassistentschappen deed zij in de Isala Klinieken te Zwolle, Igogwe Hospital te Tanzania en het Sint Lucas Andreas Ziekenhuis te Amsterdam. Vanaf september 2010 heeft zij gedurende twee en een half jaar als arts-onderzoeker gewerkt bij de Trauma Unit, Afdeling Chirurgie onder leiding van prof. Dr. J.C. Goslings hetgeen heeft geresulteerd in dit proefschrift. Na een half jaar reizen door Zuid-Amerika, heeft zij een jaar gewerkt als arts niet in opleiding tot specialist (ANIOS) op de afdeling chirurgie van het Sint Lucas Andreas Ziekenhuis te Amsterdam. Op 1 januari 2015 is zij gestart met haar opleiding tot chirurg in het VUmc/Zaans Medisch Centrum (Dr. D.L. van der Peet/ dr. F.C. den Boer).