Effect of whole-body CT during trauma resuscitation on survival: a retrospective, multicentre study

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Summary

Background **The number of trauma centres using whole-body CT for early assessment of primary trauma is increasing. There is no evidence to suggest that use of whole-body CT has any effect on the outcome of patients with major trauma. We therefore compared the probability of survival in patients with blunt trauma who had whole-body CT during resuscitation with those who had not.**

Methods **In a retrospective, multicentre study, we used the data recorded in the trauma registry of the German Trauma Society to calculate the probability of survival according to the trauma and injury severity score (TRISS), revised injury severity classification (RISC) score, and standardised mortality ratio (SMR, ratio of recorded to expected mortality) for 4621 patients with blunt trauma given whole-body or non-whole-body CT.**

Findings **1494 (32%) of 4621 patients were given whole-body CT. Mean age was 42·6 years (SD 20·7), 3364 (73%) were men, and mean injury-severity score was 29·7 (13·0). SMR based on TRISS was 0·745 (95% CI 0·633–0·859) for patients given whole-body CT versus 1·023 (0·909–1·137) for those given non-whole-body CT (p<0·001). SMR based on the RISC score was 0·865 (0·774–0·956) for patients given whole-body CT versus 1·034 (0·959–1·109) for those given non-whole-body CT (p=0·017). The relative reduction in mortality based on TRISS was 25% (14–37) versus 13% (4–23) based on RISC score. Multivariate adjustment for hospital level, year of trauma, and potential centre effects confirmed that whole-body CT is an independent predictor for survival (p≤0·002). The number needed to scan was 17 based on TRISS and 32 based on RISC calculation.**

Interpretation **Integration of whole-body CT into early trauma care significantly increased the probability of survival in patients with polytrauma. Whole-body CT is recommended as a standard diagnostic method during the early resuscitation phase for patients with polytrauma.**

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Introduction

Improvements in technology have brought about a change in the use of CT in trauma treatment. The introduction of spiral CT into clinical routine in the early 1990s has revolutionised diagnostic radiology.[1] In 1998, the introduction of multislice CT, with up to eight-fold reduction in scan times (data acquisition time), made whole-body CT technically feasible,[2,3] leading to considerations of how to integrate it as a screening technique early in trauma-room treatment.[4–7] The process quality of whole-body CT has been proven in several studies[4,6–14] that confirm its feasibility, high diagnostic safety, and substantial reduction in scan time. Whether the advantages of this technique justify its use against cost and radiation exposure is controversial.[15,16] Nevertheless, an increasing number of trauma centres is using it during the early resuscitation phase, even in haemodynamically unstable patients, because it is thought to be an effective method. To the best of our knowledge, whole-body CT was first reported to be feasible during early trauma care in 1997 by Löw[17] and in 2001 by Ptak[6] and their colleagues. In five consecutive, haemodynamically stable patients with trauma, Ptak[6] showed that single-pass whole-body CT was safe. This safety was also confirmed in other studies.[4–8,10,13,18] Multislice whole-body CT is time saving compared with conventional radiological diagnostic techniques, such as ultrasonography, radiography, or non-multislice CT.[4,6,7,10,12] However, to date, the benefit of whole-body CT on mortality in patients with major trauma has not yet been proven. We assessed whether whole-body CT during trauma-room treatment has an effect on the mortality of severely injured patients. We postulated that whole-body CT has a positive effect on mortality in patients with trauma.

Methods

Data gathering

The trauma registry of the German Trauma Society was started in 1993 by the society's Working Group on Polytrauma to prospectively gather multicentre data about people with polytrauma living in German-speaking countries (Germany, Austria, and Switzerland). Parameters for prehospital and trauma-room treatments, and subsequent treatment in the intensive care unit, are continuously inputted into a web-based data server. Every patient admitted to one of the participating trauma hospitals with an injury severity score of at least 16 or

who has been treated in the intensive care unit is recorded for the registry. Data are submitted to a central database that is hosted by the Institute for Research in Operative Medicine at the University of Witten/Herdecke, Cologne, Germany. Irreversible data anonymity is guaranteed for the patient and participating hospital. The registry records epidemiological, physiological, laboratory, diagnostic, operative, interventional, and intensive-care medical data, and injury-severity scores and outcome data.[19] The specific parameter whole-body CT has been recorded since 2002. We therefore analysed the database for 2002–04, containing information on 9259 patients.

Inclusion criteria were blunt trauma, injury-severity score of at least 16, and available information about whole-body CT during trauma-room treatment. Only those patients who were admitted directly from the incident scene, and not transferred from other hospitals, were included. 196 patients with penetrating trauma were excluded. This study has received the full approval of the ethics committee of the Ludwig-Maximilians-University of Munich, Germany.

Whole-body CT is an unenhanced CT of the head followed by contrast-enhanced CT of the chest, abdomen, and pelvis, including the complete spine. It can be done as single-pass or segmented whole-body CT. By contrast, no CT or only dedicated CT of one or combined body regions was done for non-whole-body CT.

Whether or not a patient received whole-body CT depended on the type of CT scanners and local emergency-department protocol. Participating hospitals were free to choose their own diagnostic algorithms. Information about the location of the CT scanner (in or near the trauma room or in the department of radiology) is not recorded in the trauma registry. Detailed information about the specific assessment protocols, such as collimation, slice thickness, and delay after injection of contrast material, were not available. The time to complete a whole-body CT is not recorded in the registry and can be estimated to take about 6–16 min, depending on the local conditions for each trauma centre.[10,12]

Statistical analysis

We did a descriptive data analysis that included a comparison of patients given whole-body CT with those given non-whole-body CT using two-sided χ^2 test and Mann-Whitney *U* test. We then did an outcome analysis to calculate the trauma and injury-severity score (TRISS), revised injury severity classification (RISC) score, and standardised mortality ratio (SMR; ratio of recorded to expected mortality). For comparison of mortality in patients given whole-body CT with those given non-whole-body CT, we chose a risk-adjusted approach (TRISS and RISC calculation). Survival was defined as survival to discharge.

TRISS was first introduced in 1983. It is used to roughly predict the probability of survival of a patient; it combines physiological and anatomical derangements that arise after injury. This score combines the revised trauma score,[20] which consists of on-the-scene Glasgow coma scale, systolic blood pressure, and respiratory rate, with the discharge diagnoses, age, and mechanism of trauma (blunt *vs* penetrating) based on the injury-severity score.[21,22] TRISS is the most widely used method for measurement of expected outcome in patients with trauma, and the probability of survival after blunt trauma is calculated with the following formula:[22]

$$1/(1+e^{-x}); x=0\cdot9544\times\mathrm{RTS}-0\cdot0768\times\mathrm{ISS}-1\cdot9052\times(\mathrm{AGE})-1\cdot2470 \quad \text{(formula 1)}$$

e is 2·7182818 (base of the natural logarithm [Euler's number]), RTS is revised trauma score, ISS is injury-severity score, and age is 0 for patients younger than 55 years, and 1 for those 55 years or older. Although TRISS is widely used, it has limitations. The main limitation is the reduced applicability due to missing physiological parameters, particularly the respiratory rate. This rate is not recorded by the emergency teams at the scene of the trauma in about 33% of cases in the trauma registry. Other variables with proven effect on the outcome, like the base excess or coagulatory parameters, are not used for calculation of TRISS.[23] When applied to the data in the registry, the TRISS-calculated prognosis is about 4–5% greater than the recorded mortality rate; therefore use of this score might result in an overestimation of the probability of death.

To increase the applicability and predictive accuracy, the Institute for Research in Operative Medicine developed the RISC score for calculation of the probability of death in patients with trauma. This score was developed with data from 2009 patients in the trauma registry (1993–2000) and has been validated for 3475 patients (2001–03). It is calculated on the basis of more variables than is TRISS (table 1). Other variables are substituted when values are missing—eg, missing partial thromboplastin time is substituted for thromboplastin time. RISC-score-adjusted outcome comparisons have been routinely reported every year by the trauma registry since 2003.[24] The probability of death is calculated with the following formula:

$$1/(1+e^{-x}); x=5\cdot0+\text{coefficients} \quad \text{(formula 2)}$$

Area under the curve of the receiver operator characteristic is 0·906 (95% CI 0·895–0·918) for the RISC score and 0·875 (0·863–0·887) for TRISS. Goodness of fit according to Hosmer and colleagues[25] is significantly better for the RISC score than for TRISS. Lefering's[26] calculations were based on valid data from about 5000 patients in the trauma registry that could be used

	Coefficient
Age (years)	
55–64	–1·0
65–74	–2·0
≥75	–2·3
New ISS (points)	
1–75 (per point)	–0·03
Head injury (AIS points)	
4	–0·5
5/6	–1·8
Limb injury (AIS points)	
5	–1·0
GCS (points)	
3–5	–0·9
PTT (s)	
40–49	–0·8
50–79	–1·0
≥80	–1·2
Base excess (mmol/L)	
–9·0 to –19·9	–0·8
≤–20	–2·7
Cardiorespiratory arrest	
Yes	–2·5
Bleeding signs (n)*	
1	–0·4
2	–0·8
3	–1·6
Constant	5·0

AIS=abbreviated injury scale. GCS=Glasgow coma scale. ISS=injury-severity score. PTT=partial thromboplastin time. *Systolic blood pressure <90 mm Hg, or haemoglobin concentration <90 g/L or ≥ 10 units of packed red blood cells.

Table 1: **Revised injury severity classification (RISC) score**

	Total (n=4621)	Whole-body CT (n=1494)	Non-whole-body CT (n=3127)	p value
Age (years)	42·6 (20·7)	42·5 (20·3)	42·7 (20·8)	0·85
Men	3364 (73%)	1098 (74%)	2267 (73%)	0·49
Prehospital				
Shock on scene (SBP <90 mm Hg)	970 (21%)	353 (24%)	616 (20%)	0·004
Intubation	2740 (59%)	1035 (69%)	1704 (55%)	<0·001
GCS on scene (points)	10·3 (4·8)	9·9 (4·8)	10·4 (4·8)	0·002
Trauma room/in hospital				
Shock on admission (SBP <90 mm Hg)	707 (15%)	260 (17%)	444 (14%)	0·005
Haemoglobin concentration (g/L)	113 (30)	110 (28)	114 (30)	<0·001
Thromboplastin time (%)	74·9 (23·3)	73·1 (22·3)	75·9 (23·8)	<0·001
Base excess (mmol/L)	–3·7 (5·0)	–4·1 (4·8)	–3·5 (5·1)	<0·001
Time from trauma-room admission to CT (min)	41·7 (33·9)	35·5 (26·5)	46·6 (37·5)	<0·001
Operation	3581 (78%)	1264 (85%)	2258 (72%)	<0·001
Massive blood transfusion until ICU (≥10 PRBC transfused)	425 (9%)	160 (11%)	266 (9%)	0·015
Multiorgan failure*	1229 (27%)	569 (38%)	644 (21%)	<0·001
Ventilation time (days)	8·7 (12·8)	10·2 (14·1)	7·9 (12·1)	<0·001
ICU stay (days)	12·5 (14·7)	14·2 (15·6)	11·7 (14·2)	<0·001
Hospital stay (days)	26·0 (30·2)	28·2 (33·4)	25·0 (28·4)	0·002
Abbreviated injury scale (≥3)				
Head	2768 (60%)	884 (59%)	1882 (60%)	0·51
Thorax	2625 (57%)	1035 (69%)	1589 (51%)	<0·001
Abdomen	1049 (23%)	390 (26%)	660 (21%)	<0·001
Extremities	1687 (37%)	614 (41%)	1073 (34%)	<0·001
Injury-severity score (points)	29·7 13·0)	32·4 (13·6)	28·4 (12·4)	<0·001
Mortality rate				
24 h	518 (11%)	146 (10%)	372 (12%)	0·038
Overall	998 (22%)	306 (21%)	691 (22%)	0·21

Data are number (%) or mean (SD), unless otherwise indicated. GCS=Glasgow Coma Scale. ICU=intensive care unit. PRBC=packed red blood cells. SBP=systolic blood pressure. *Defined as organ failure of two systems of >2 sepsis-related organ-failure assessment-score points for at least 2 days.[28]

Table 2: **Characteristics of patients with polytrauma with information about CT during trauma-room treatment**

for calculation of TRISS or RISC score, or both. Comparison of these two scores shows better precision, discrimination, and calibration for the RISC score than for TRISS.[24–27]

RISC and TRISS scores were used to deduce the expected mortality for inclusion in calculation of SMR. If SMR is 1, then the calculated mortality rate is identical to the recorded rate; less than 1 means that more patients than expected survive; and a ratio greater than 1 means fewer patients than predicted survive. We calculated 95% CIs when appropriate. Significance was assessed at $p<0·05$. We did the statistical analysis using SPSS (version 15.0).

To find out whether whole-body CT is significantly associated with the risk of death, we calculated logistic regression models in which this CT had been tested with the well known prognostic indices of TRISS, RISC score (models 1 and 2), and other potential interfering factors like hospital level (I, II, or III) or year of the trauma (models 3 and 4). We did sensitivity analysis for potential centre effects by assessing whole-body CT×hospital interaction terms, with inclusion of the term hospital as an independent predictor in the logistic regression models. The dependent (target) variable was hospital-related mortality. To correctly include these probabilities into the logistic model, we transformed them with the inverse logistic function:

$$x=\ln[1/p-1]$$

in which p is the score probability and x is identical to that in formulas 1 and 2 into values that were appropriate for logistic modelling. We analysed each prognostic score separately.

Role of the funding source

There was no funding for this study. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

4621 of 9259 patients met the inclusion criteria. 1494 (32%) of 4621 patients underwent whole-body CT during early resuscitation phase, 3127 (68%) did not. 697 (22%) of 3127 patients assigned to non-whole-body CT did not undergo any kind of CT and 2430 (78%) were given selective organ CTs (2024 [83%] head, 863 [36%] thorax, 627 [26%] abdomen, 416 [17%] pelvis, and 960 [40%] spine).

The mean time from trauma-room admission to starting whole-body CT was significantly shorter than that for non-whole-body CT (table 2). We did not note any adverse effects that could be attributed to whole-body CT. The TRISS method could be applied to 2259 of 4621 patients meeting the inclusion criteria. 800 patients with TRISS prognosis received whole-body CT, 1459 did not. The recorded mortality rate for patients given whole-body CT was 138 (17%) and was significantly lower than the 186 (23%) predicted with TRISS (p<0·001). The absolute risk reduction was 5·9%, representing a relative reduction of 25% (95% CI 14–37). For 1459 patients given non-whole-body CT, the recorded mortality rate was 255 (18%) and higher than 250 (17%) predicted with TRISS (p=0·66). The SMR for 800 patients given whole-body CT was 0·745 (0·633–0·859), which meant that the recorded mortality rate was significantly lower than that predicted with TRISS. The SMR for 1459 patients given non-whole-body CT was 1·023 (0·909–1·137) with a recorded mortality rate higher than predicted with TRISS (figure). The number needed to treat or, better, the number needed to scan based on TRISS was 17 for whole-body CT.

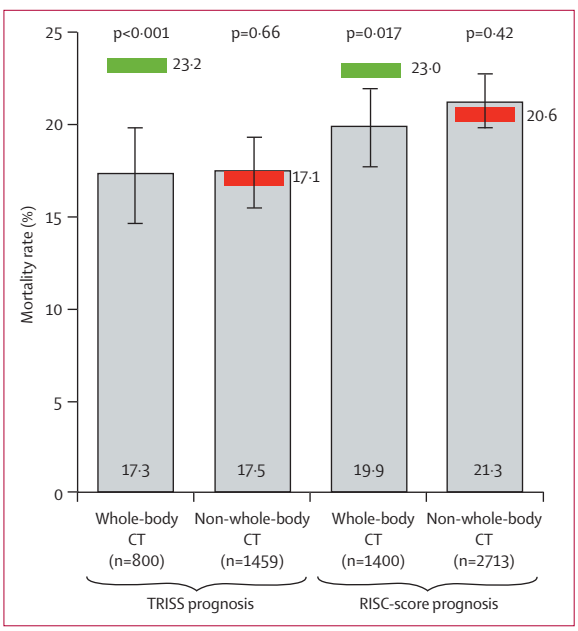

Figure: **Effect of whole-body CT on outcome**
Grey columns represent the recorded mortality rates. Error bars represent 95% CI. Green bars show that the recorded mortality rates are lower than the predicted rates. Red bars show that the recorded mortality rates are higher than the predicted rates. RISC=revised injury severity classification. TRISS=trauma and injury severity score.

	Regression coefficient β	p value	Odds ratio (e^{β}; 95% CI)
Model 1: TRISS+whole-body CT (n=2259)			
TRISS*	−0·62	<0·001	0·54 (0·51–0·58)
Whole-body CT	−0·42	0·002	0·66 (0·50–0·86)
Constant	−0·34	<0·001	..
Model 2: RISC+whole-body CT (n=4113)			
RISC score*	0·92	<0·001	2·50 (2·35–2·66)
Whole-body CT	−0·37	<0·001	0·69 (0·58–0·85)
Constant	−0·02	<0·81	..

RISC=revised injury severity classification. TRISS=trauma and injury severity score. *Inverse logistic transformation of the predicted outcome probability of TRISS (survival) or RISC score (mortality).

Table 3: **Logistic regression models 1 (TRISS+whole-body CT) and 2 (RISC score+whole-body CT)**

The RISC calculation could be done in 4113 patients. 1400 patients with RISC prognosis received whole-body CT, 2713 did not. The recorded mortality rate for patients given whole-body CT was 279 (20%) and thus significantly lower than 322 (23%) predicted with the RISC score (p=0·017). The absolute risk reduction was 3·1%, representing a relative reduction in mortality of 13% (95% CI 4–23). The recorded mortality rate was 578 (21%) of 2713 patients given non-whole-body CT and higher than 559 (21%) predicted with the RISC score (p=0·42). The SMR for 1400 patients given whole-body CT was 0·865 (0·774–0·956), which meant that the recorded mortality rate was significantly lower than that predicted with the RISC score. The SMR for the 2713 patients given non-whole-body CT was 1·034 (0·959–1·109); therefore, the recorded mortality rate was higher than predicted with the RISC score (figure). The number needed to scan based on the RISC score was 32 for whole-body CT. The non-overlapping CIs of SMR for TRISS and RISC-score calculations show that the recorded differences are significant.

Logistic regression analysis of whole-body CT with the well known prognostic indices of TRISS or RISC score showed that this CT is an independent predictor for survival that significantly adds predictive power to the model (p≤0·002). Table 3 shows the results of models 1 (TRISS+whole-body CT) and 2 (RISC score+whole-body CT). The size of the effect suggests that the odds of survival could be increased by about a third if whole-body CT is done. The same effect was noted with models 3 and 4 for logistic regression analysis (table 4; table 5) even with additional adjustment for hospital level and year of trauma. The findings remained stable and robust even after adjustment for potential centre effects.

Discussion

The probability of survival, based on TRISS, RISC-score, and SMR, increased significantly for patients given whole-body CT compared with non-whole-body CT. The mean injury-severity score for patients with severe blunt trauma in our study was similar to that in other studies on

	Regression coefficient β	p value	Odds ratio (e^{β}; 95% CI)
TRISS*	–0·62	<0·001	0·54 (0·51–0·58)
Whole-body CT	–0·42	0·002	0·66 (0·50–0·86)
Level			
I (reference)	..	0·67	..
II	0·08	0·62	1·08 (0·80–1·47)
III	0·38	0·44	1·46 (0·57–3·76)
Year			
2002 (reference)	..	0·73	..
2003	0·11	0·50	1·12 (0·82–1·52)
2004	–0·01	0·99	1·00 (0·74–1·35)
Constant	–0·39	0·002	..

TRISS=trauma and injury severity score. *Inverse logistic transformation of the TRISS-predicted probability of survival.

Table 4: **Logistic regression model 3 (TRISS+whole-body CT+level of hospital+year) based on data from 2259 patients**

	Regression coefficient β	p value	Odds ratio (e^{β}; 95% CI)
RISC score*	0·92	<0·001	2·50 (2·35–2·66)
Whole-body CT	–0·38	0·001	0·69 (0·55–0·85)
Level			
I (reference)	..	0·96	..
II	0·11	0·93	1·01 (0·79–1·30)
III	–0·12	0·81	0·89 (0·35–2·29)
Year			
2002 (reference)	..	0·68	..
2003	0·06	0·62	1·06 (0·84–1·35)
2004	–0·05	0·70	0·95 (0·75–1·22)
Constant	–0·02	0·82	..

RISC=revised injury severity classification. *Inverse logistic transformation of the RISC-score-predicted probability of death.

Table 5: **Logistic regression model 4 (RISC+whole-body CT+level of hospital+year) based on data from 4113 patients**

whole-body CT.[7,12] Patients given whole-body CT had a significantly higher injury-severity score than did those given non-whole-body CT (table 2). Furthermore, the mean time from trauma-room admission to beginning whole-body CT was significantly shorter than for an organ-selective CT. This difference could be explained by the fact that more CT scanners are located inside or near the trauma room and an increasing number of trauma centres do whole-body CT during the early resuscitation phase. Of note, every fifth patient who underwent whole-body CT was in shock at the scene of the trauma and every sixth patient at the time of trauma-room admission.

To estimate radiation exposure, an effective radiation dose is assumed to be 10–20 mSv for a whole-body CT, 5–16 mSv for a selective-organ CT, and 2 mSv for a conventional radiography series (chest, vertebral column, pelvis).[29] However, the effective dose for particular organs can accumulate and thereby potentially increase an individual's risk of cancer.[30] Despite the patient's size, the dose is strongly dependent on parameters and protocols used for CT.[14,31] Comparison of different protocols for whole-body CT shows that those for single-pass acquisition result in lower radiation exposure than do segmented, partially overlapping protocols.[14,31]

Whole-body CT is associated with greater radiation exposure than is CT targeted to a particular organ and anatomical area. The potentially harmful effects of increased radiation exposure have to be weighed against the better diagnostic accuracy of the whole-body technique. Even if increased risk of developing cancer years or decades later cannot be neglected, a swift, accurate, and comprehensive diagnosis is mandatory in critically injured patients. To justify the increased radiation exposure, the potential gain in diagnostic safety should ideally result in an increased probability of survival. Salim and colleagues[13] showed that whole-body CT resulted in a change of treatment in 19% of 1000 patients without obvious external signs of injuries. Deunk and co-workers[32] reported that chest or abdominal CT resulted in a change of treatment in up to 34% of patients with blunt trauma.

We chose a risk adjustment method by calculating TRISS, RISC score, and SMR to compare patients given whole-body CT with those given the non-whole-body technique. However, score-based prognosis can only adjust for injury severity. Additional confounding factors could be the dedication of a centre to trauma care, level of hospital, experience of surgeons, or therapeutic improvements over time. Not all of these factors could be measured validly and thus could not be accounted for. But multivariate analysis that takes into account the hospital level and year of trauma showed that the association of whole-body CT with improved outcome is still substantial. We are aware that our findings show associations rather than causalities. Our findings suggest that integration of whole-body CT into the early trauma resuscitation phase has an advantage on the endpoint of survival.

The crucial factor in whole-body CT is not the exposure of radiation but the early realisation and implementation of the findings to the critically injured patient. We postulate that the earlier the emergency team knows the definitive pattern of injury, the sooner a prioritised therapeutic plan can be developed and realised for the benefit of the patient. Therefore whole-body CT, if done early, can replace conventional radiography with a considerable amount of time saved.[33]

Use of whole-body CT does not mean that use of standard techniques, such as ultrasonography and conventional radiography, will decrease. These techniques are well established and reasonable, and should be used as adjuncts to whole-body CT or as a backup in case of CT failure (ie, complete shutdown or breakdown of CT before or during the procedure). In our opinion whole-body CT

is the most comprehensive diagnostic method and should be part of a modified advanced trauma life-support-based treatment.

To achieve a synergistic effect that increases the probability of survival in major trauma, an existing, functional, and structured trauma room work flow is needed in which early whole-body CT is an integral part. Whole-body CT without an effective, structured, and targeted resuscitative treatment will not increase the survival rate.

Our results show the importance of having a CT scanner near the trauma room. In our opinion, when planning or rebuilding emergency departments, CT scanners should be placed close to or, at best, in the trauma room.

Our study has several limitations that might bias the results. It was not done prospectively. Because of missing data in the trauma registry, calculations of TRISS could be done in only 2259 (49%) and RISC score in 4113 (89%) of 4621 patients. Since the participating hospitals choose their own diagnostic workup, indications for or against whole-body CT were not clearly defined. The registry does not have information about structural differences of the participating hospitals, such as the location of the CT scanner and transportation times between the trauma room and CT suite. We also do not have information about CT protocols, type of contrast enhancement, or any data about radiation doses for the hospitals. Furthermore we do not know which hospital, and to what extent, has implemented the principles of advanced trauma life support. Potentially different intercentre consistency in grading injuries (abbreviated injury scale or injury-severity score) might also bias our results. The substantial geographic and structural differences between regions and federal states in Germany might have additional and unquantifiable effects on our results. Furthermore, residual confounding could be caused by preferential selection of likely survivors in centres with better equipment or highly developed protocols to select and undertake whole-body CT in patients who might benefit, or by the level of experience of the attending doctors within a centre to prefer whole-body CT and hence provide better care to those patients given this CT.

The results of our study need to be confirmed in a randomised controlled trial in which the safety issues (radiation doses), treatments as a consequence of whole-body CT, and the costs and benefits are rigorously and prospectively assessed.

Despite these limitations, our results indicate that the probability of survival for patients with major trauma can be significantly increased by use of whole-body CT. On the basis of our findings, we recommend that whole-body CT should be integrated into the early resuscitation phase of severely injured patients as a standard and basic diagnostic method.

Contributors

SHW and KGK participated in the idea, planning, data analysis and interpretation, statistical analysis, and writing the report. RL participated in the planning, data analysis and interpretation, statistical analysis, and writing the report (methods, results, and discussion). LMQ participated in the data analysis and interpretation, searching for publications, and writing the report. MK participated in data interpretation, searching for publications, and writing the report (radiological part). MVK participated in data interpretation, language support, and writing the report. KJP and MR participated in data interpretation and writing the report (radiological part). WM participated in data analysis and interpretation, statistical analysis, and writing the report. All authors have seen and approved the final version of the report.

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Participating hospitals

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Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

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Effect on survival of whole-body CT during trauma resuscitation

Stefan Huber-Wagner and colleagues (April 25, p 1455)[1] report a reduction in mortality of about 30% in blunt trauma patients who received whole-body CT compared with those who received no CT or non-whole-body CT. A large proportion of this apparently protective effect might be attributable to immortal time bias.[2,3]

Patients who received whole-body CT necessarily had to survive until the whole-body CT was done, so they were artificially protected from death between admission to the trauma room and the time of CT ("immortal person time"). Patients who died before having received a CT were by definition assigned to the comparison group of patients without whole-body CT. About 25% of deaths have been reported to occur within the first hour after arrival at the emergency unit, and such deaths therefore account for an important proportion of the total number of fatal events.[4]

Since immortal time bias is introduced by study design and not by confounding, it cannot be overcome by statistical adjustment. One way to avoid this bias is to consider person-time instead of number of patients, and to consider the time-varying exposure status (whole-body CT *vs* no whole-body CT) in a Poisson or a Cox proportional hazard model.[3]

I declare that I have no conflicts of interest.

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Stefan Huber-Wagner and colleagues[1] conclude that "whole-body CT is recommended as a standard diagnostic method during the early resuscitation phase for patients with polytrauma." But should they really make this statement without any valid information about its efficacy and effectiveness? We have made mistakes in this regard in the past. Focused abdominal sonography for trauma, originally praised to the skies, turned out to have an unacceptably low sensitivity[2] and did not prove superior to other algorithms.[3]

Huber-Wagner and colleagues are reluctant to discuss the limitations of their database and analyses. They do not take into account the decline in trauma mortality since the mid-1990s, before the introduction of pan-CT. The chosen interval of observation seems tight and arbitrary—why not use the full range of consecutive data available from 1993 to 2008?

The numbers needing to scan indicate that between 16 of 17 and 31 of 32 patients do not benefit from an intervention that increases their lifetime risk of cancer[4] and exposes them to iodine-containing contrast agents. In another study, emergency physicians deemed 18–41% of CT scans unnecessary; none of 51 injuries quasi-missed in 284 patients required immediate therapeutic action.[5]

The multicentre randomised controlled trial proposed in the Discussion is mandatory but half-hearted, since Huber-Wagner and colleagues draw conclusions that apparently violate the equipoise principle. We should use the results not to uncritically expand the indication for whole-body scanning, but to investigate the appropriateness of current triage criteria, and related changes in therapeutic behaviour. This will ensure that pan-CT inures to the benefit of those who need it most.

I declare that I have no conflicts of interest.

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The Article by Stefan Huber-Wagner and colleagues[1] deals with a topic that is still controversial and therefore of substantial clinical relevance. Because of this controversy, however, the conclusions drawn by Huber-Wagner and colleagues cannot be derived from the presented data without caveats.

We are particularly disturbed by the differences in sample structure of the two groups compared. Patients who received whole-body CT were on average more severely injured than those who received non-whole-body CT. Survival after 24 h was significantly better in patients undergoing whole-body CT, but was this improvement really related to the primary use of whole-body CT?

Infrastructure and level of treatment vary between the participating hospitals and might be better in facilities that routinely do whole-body CT than in those that do not. This enhanced environment might have a strong influence on patients' outcome and could have biased the data towards Huber-Wagner and colleagues' hypothesis. They do not provide any data on the indications for or against whole-body CT in the various hospitals.


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Other researchers have shown that the probability of survival in severely injured patients who present with haemorrhagic shock decreases at a rate of 1% for every 3 min delay of surgery.[2] Rapid laparotomy and surgical bleeding control is of primary importance. The critical factor in abdominal trauma is haemodynamic instability.[3] Despite the presented data, we cannot see why primary whole-body CT should be done in polytraumatised patients who present with haemorrhagic shock and sonographically detected intra-abdominal fluid. We therefore regard any recommendation to do whole-body CT in haemodynamically instable patients as contraindicated or even dangerous.

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Stefan Huber-Wagner and colleagues[1] report an increase in the probability of survival after use of total-body CT scanning, compared with dedicated CT, in multitrauma patients.

As with other publications on total-body CT, the results seem promising, but owing to methodologically suboptimum designs, the authors suggest doing more prospective research to provide better evidence on clinical outcomes, cost effectiveness, and radiation exposure.[1–3]

Because of our interest in early CT scanning[4,5] we designed a randomised controlled trial in which we will compare immediate total-body CT without previous conventional radiography with dedicated CT after conventional radiography. Since retrospectively calculated trauma scores (eg, the injury severity score) cannot be used in daily practice, inclusion criteria are based on vital signs and injury pattern. This design also provides an assessment of potential overtriage that could result in unnecessary radiation exposure. To ensure maximum patient safety, participating hospitals are required to have a CT scanner, resuscitation possibilities, and conventional imaging equipment in the trauma room.

To include the required 1078 patients (power calculation based on 30-day mortality), we have contacted several European trauma centres. Unfortunately, few hospitals have the facilities described above. Centres meeting the requirements had already adjusted their protocols and were not willing to randomise patients to the standard imaging strategy.

Randomised trials produce the best evidence. We call for international collaboration in multicentre randomised controlled trials in order to obtain the required level of evidence for implementation of this diagnostic strategy.

The REACT 2 study group consists of: T P Saltzherr, K J Ponsen, J S K Luitse, L F M Beenen, C P Henny, M W Hollmann, M G W Dijkgraaf, J B Reitsma, and J C Goslings. We declare that we have no conflicts of interest.

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Authors' reply

We agree with Frank Andersohn that immortal time bias could have affected our study. He is right in stating that patients who received whole-body CT had to survive until the procedure was done. However, as stated in the results, only 22% of patients in the non-whole-body CT group received no CT at all. This means that 78% *did* receive some form of dedicated-organ CT, so in fact most of the patients in the non-whole-body CT group also had to survive until selective-organ CT.

To eliminate this potential bias, we recalculated our results excluding all patients who died within the first hour after hospital admission (mean time to whole-body CT was 35 min, see table 2 of the original paper). In fact those early deaths were more common in the non-whole-body CT group (n=58 *vs* n=8). However, these patients also had a very bad prognosis: the average predicted mortality rate was 75%. Thus exclusion of these cases lowered both predicted and observed mortality rates in the non-whole-body CT group (observed 19·6% *vs* expected 19·4%, based on the revised injury severity classification score), whereas the results in the whole-body CT group remained virtually unchanged (19·5% *vs* 22·7%, respectively). Similar results are obtained if the trauma and injury severity score is used. This analysis shows that the potential immortal time bias only marginally affects our findings.

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Peter Giannoudis asks why we chose the period 2002–04 when trauma mortality has been declining since the mid-1990s. As mentioned in the Methods, the use of whole-body CT has been recorded in the trauma registry only since 2002. Furthermore, during the period considered here many hospitals introduced whole-body CT in their diagnostic strategy so that there are cases both with and without whole-body CT from the same hospital. Recalculations of the observed effect of whole-body CT on data from 2002 to 2007 using the same methods confirmed the presented effect.

Giannoudis also addresses the important issue of radiation. However, in our opinion, the survival of every 17th or 32nd patient owing to whole-body CT outweighs the cancer risk of about 1:1250.[1]

Peter Strohm points out that infrastructure and level of treatment varied between the participating hospitals. We addressed this important issue in our logistic regression model (tables 4 and 5) and by adjustment for potential centre effects. The findings remained stable and robust in all calculated models, showing that there is an independent and positive effect of whole-body CT on survival. However, Strohm is right in stating that the registry is not able to give detailed information about the indications for whole-body CT, which might vary in the participating hospitals (see Methods). This is a clear and discussed limitation of our study. The group differences mentioned by Strohm are typical of non-randomised comparisons. We therefore did not compare mortality rates directly but used a risk-adjusted method.

Furthermore Strohm addresses the issue of shock. We agree with the important findings by Clarke and colleagues.[2] However, we point out that, if done, whole-body CT has to be really fast. It has been shown that it is possible to acquire contrast-enhanced whole-body CT within 3–6 min.[3,4] We think that the information derived from the whole-body CT scan can be very important for further management. Is there any bleeding? Where exactly is it? Is there more than one source? Is there an (additional) thoracic or intracranial haemorrhage? Mahoney showed that the cause of hypotension in blunt trauma patients is non-haemorrhagic in up to 50% of cases.[5] By answering these questions, whole-body CT, if done early and quickly, might help to apply rational damage control surgery to the best of the patients.

Finally, we completely agree with T P Saltzherr and J C Goslings that a randomised controlled trial would provide the best evidence for the implementation of whole-body CT as a routine diagnostic strategy. We strongly support the efforts of the REACT 2 study group and request all interested hospitals to take part in their prospective and randomised assessment of whole-body CT during early trauma care.

We declare that we have no conflicts of interest.

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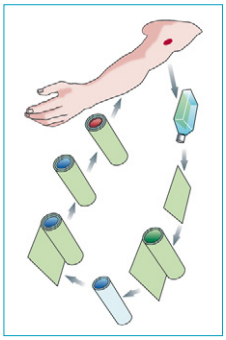
Haemodialysis access via tissue-engineered vascular graft



Todd McAllister and colleagues' Article (April 25, p 1440)[1] on the use of autologous tissue-engineered vascular grafts in patients on haemodialysis is a seminal paper on the use of bioengineered tissue in clinical medicine. But we were somewhat surprised by the frequency of aneurysms or graft dilatations in this small cohort after a short time of use. We wonder whether there is a relation between the dilatation of the graft and the underlying kidney disease, in particular autosomal dominant polycystic kidney disease (ADPKD).

ADPKD is a systemic disease: besides the kidney cysts, other structures are involved, particularly the arteries, with aneurysms of cerebral arteries and an increased risk of aortic dissection.[2] Additionally, arteriovenous fistulae in patients with ADPKD are wider (median of 12 mm) than in patients with other renal diseases (median of 8 mm).[3]

The tissue-engineered graft is produced from fibroblast culture. We have found an abnormal phenotype in fibroblast cultured from *Pkd2* knockout mice.[4] 30% of the fibroblasts had an abnormal number of centrosomes. Abnormal mitosis associated with over-duplication of centrosomes can lead to an abnormal extracellular matrix. The composition of this structure in ADPKD is abnormal.[5] These extracellular matrix abnormalities related to ADPKD could explain the graft dilatation seen in McAllister and colleagues' patients.

In summary, to anticipate vascular complications in this new kind of graft, we think it is important to pay attention to the underlying kidney diseases of the patients who provide the fibroblasts for graft production.

We declare that we have no conflicts of interest.

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