

STEN SAAR

Epidemiology of severe injuries
in Estonia



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Department of Surgery, Institute of Clinical Medicine, Faculty of Medicine,
University of Tartu

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*To my beloved wife Liina-Kadi and
daughters Helena Iris and Anette Karolin*

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LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following original publications referred to the text per their Roman numerals:

- I Saar S, Merioja I, Lustenberger T, Lepner U, Asser T, Metsvaht T, Ilmoja ML, Kukk L, Starkopf J, Talving P. **Severe Trauma in Estonia: 256 Consecutive Cases Analysed and the Impact on Outcomes Comparing Two Regions.** European Journal of Trauma Emergency Surgery 2016;42: 497–502.
- II Saar S, Sokirjanski M, Junkin LK, Laos J, Laar AL, Merioja I, Lepner U, Kukk L, Rimmelgas A, Asser T, Innos K, Starkopf J, Talving P. **Evolution of Severe Trauma in Estonia Comparing Time Segments of Early versus Established Independence of the State.** European Journal of Trauma Emergency Surgery 2017;43:791–796.
- III Saar S, Lomp A, Laos J, Mihnoviř V, řalkauskas R, Lustenberger T, Väli M, Lepner U, Talving P. **Population-based Autopsy Study of Traumatic Fatalities.** World Journal of Surgery 2017;41:1790–1795.
- IV Saar S, Brinck T, Laos J, Handolin L, Talving P. **Severe Blunt Trauma in Finland and Estonia: Comparison of Two Regional Trauma Repositories.** European Journal of Trauma Emergency Surgery 2019 (in press).

Contribution of Sten Saar to the original publications:

Papers I–IV: Participated in the study design, data collection and interpretation, data analysis, statistics, writing, and publishing.

ABBREVIATIONS

AIS	Abbreviated Injury Scale
ATLS	Advanced Trauma Life Support for Doctors
ASSET	Advanced Surgical Skills for Exposure in Trauma
BAL	Blood alcohol level
CCI	Charlson's comorbidity index
DGU [®]	TraumaRegister DGU [®]
DATC	Definitive Anesthetic Trauma Care
DSTC	The Definitive Surgical Trauma Care
EDH	epidural hematoma
GCS	Glasgow coma scale
HLOS	hospital length of stay
HTR	Helsinki University Hospital trauma registry
ICU-LOS	intensive care unit length of stay
IPH	intraparenchymal hemorrhage
ISS	Injury Severity Score
IVC	inferior vena cava
IVH	intraventricular hemorrhage
MVA	motor vehicle accident
NTDB [®]	National Trauma Data Bank [®]
NEMC	North Estonia Medical Centre
NISS	New Injury Severity Score
RISC	Revised Injury Severity Classification
RR	respiratory rate
RTS	Revised Trauma Score
SAH	subarachnoidal hemorrhage
SBP	systolic blood pressure
SDH	subdural hematoma
SMR	standardized mortality ratio
TARN	The Trauma Audit and Research Network
TBI	traumatic brain injury
TCH	Tallinn Children's Hospital
TRISS	Trauma Score – Injury Severity Score
TTR	Trauma repository at the NEMC in Tallinn
TUH	Tartu University Hospital

1. INTRODUCTION

Traumatic deaths contribute to more years of life lost globally compared to cancer and cardiac related deaths combined (Trunkey 1983). It is estimated, that after every six seconds someone deceases secondary to an injury accounting for more than five million trauma related deaths every year exceeding even fatalities secondary to HIV, tuberculosis and malaria (WHO 2015) (Figure 1). Unintentional injuries are the leading cause of death in the age group of 1–44 years. In the age group of 15–34 years, unintentional injuries, homicides, and suicides are the top three causes of death (CDC 2017). Likewise, the economic burden of injury to society is staggering as a significant proportion of patients are contributing to economic revenues while they suffer permanent disability or death due to traumatic insults.

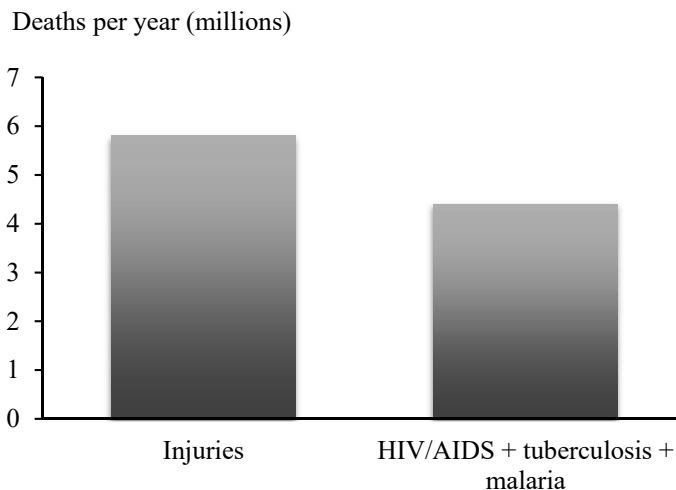


Figure 1. Fatalities secondary to injuries and HIV/AIDS, TB and malaria (WHO, Injuries and Violence: the facts, Global burden of disease, 2004).

Injury-related deaths in Estonia are among highest in the European Union per the EuroSafe reports comprising 7–11% of all causes of death in recent years in Estonia (EuroSafe 2016, EuroSafe 2014, EuroSafe 2013). Thus, injury related deaths are significant public health concern locally, regionally and in a global perspective.

ISS is most widely utilized and recognized trauma severity score in a scientific literature based on anatomic indices (Baker, et al. 1974). ISS >15 is defined as severe trauma and patients with severe injury burden have considerably better survival outcomes when treated at designated trauma centers (Demetriades, et al. 2006).

Estonia has two designated trauma centers treating most of the severely injured patients including NEMC with TCH in the Northern region involving a

catchment area of 25 000 km² with estimated population of 800 000 inhabitants. Tartu University Hospital (TUH) being the referral trauma center in the Southern region comprises a population of 500 000 within a 20 000 km² catchment area. Trauma system in Estonia has evolved dramatically since Estonia regained independence in 1991 after dissolution of Soviet Union. As an undeveloped country, the trauma system was poorly designed and scarcely equipped during nineties with a very high rate of violent crime at that time. Nevertheless, Estonian trauma system has developed significantly in all aspects with a modern pre-hospital system accessing to all patients within 30-min time interval, introduction of damage control resuscitation and surgery, improved intensive care and rehabilitation. Also, the most important trauma courses including ATLS (since 2015), DSTC & DATC (since 2017) and ASSET (since 2018) have been introduced recently (American College of Surgeons 1980, IATSIC 2015, American College of Surgeons 2010).

However, studies involving severely injured patients (ISS >15) in Estonia were lacking. Thus, the studies involved in the thesis are the pioneering investigations including patients with severe injuries per ISS with comparison of time periods, trauma centers, pre-hospital deaths, and with other countries. Also, as Estonia is relatively small country with few designated trauma centers and one common forensic medicine database autopsy studies with population-based perspective are possible.

2. REVIEW OF THE LITERATURE

2.1. Trauma Scorings

ISS is most widely utilized trauma severity score in a scientific literature based on anatomic indices (Baker, et al. 1974) ISS is based on the AIS score, which divides injuries to six regions of body: head-neck, face, chest, abdomen, pelvis-extremities, and body surface (Gennarelli, Wodzin ja Association for the Advancement of Automotive Medi 2008). All injuries in every region are classified in a six-point scale with higher number correlating with more severe injury. To calculate the ISS the highest AIS score in the three most severely injured ISS body regions is squared and added for the final ISS score. ISS score ranges between 1 and 75 and higher score correlates with higher morbidity and mortality. ISS >15 definition of severe trauma is globally accepted and widely utilized since 1974 after introduction by Baker and colleagues (Baker, et al. 1974). Accordingly, the ISS >25 defines critical injury burden. ISS permits to compare outcomes of patients treated at different hospitals or different time periods with similar injury burden. However, ISS has some well-known limitations with most important being that different injuries in one region are not weighted in. Also, ISS is not useful as a triage tool as all injuries must be recognized for calculation (TRAUMA.ORG 2006). Nevertheless, despite some weaknesses as with most of medical scoring systems the ISS is still extensively used and allows comparison between different settings and with former studies.

The RTS score is another widely utilized trauma scoring based on three first measured physiological parameters including GCS, SBP and RR (Champion, Sacco ja Carnazzo, et al. 1981, Champion, Sacco ja Copes WS, et al. 1989). RTS ranges between 0 and 7.841 with lower score correlating with worse outcomes, however, inconsistency of measurement cut-offs of the physiological variables and frequently missing variables affects the use of this score for comparison between different trauma settings. Nevertheless, the RTS is part of the TRISS score, which adds ISS, RTS, patient's age, and mechanism of injury (blunt or penetrating) into a computed based logarithmic equation to calculate probability of survival between 0 and 100% (Boyd, Tolson ja Copes 1987). Thus, TRISS methodology permits to calculate survival rate for certain cohort of injured patients and compare it with actual crude mortality showing if the real outcomes are worse or better per prediction. TRISS is relatively easy to use and, thus, has been utilized for many decades to compare improvements in time and between trauma centers. TRISS methodology is criticized for the simplistic dichotomous stratification of age variables and low performance for certain mechanism of injuries (Kennedy, Grant ja Blackwell 2001).

Many new scoring systems have been adopted including NISS or RISC score, however, the well-known classical trauma scores ISS, RTS and TRISS persist as the globally utilized standardized measures of injury severity (Lefering 2009, Lavoie, et al. 2004).

2.2. Demographics and Outcomes of patients with Injury Severity Score >15

Overall consensus exists that severely injured patients should be treated at designated trauma centers. A large study by Demetriades and co-authors involving more than 130 000 patients with ISS >15 noted significantly lower adjusted mortality rate at Level I trauma centers in USA compared to lower level or undesignated trauma centers (Demetriades, et al. 2006). Per the study by Demetriades et al., the overall injury mortality was 14.9% and 16.8% at Level I centers and lower level or undesignated trauma centers, respectively. Penetrating trauma accounted 11.2% of cases and every third patient (33.2%) was critically injured.

In the European setting, the outcomes are variable across the regions. A study from Switzerland showed relatively high overall mortality at 26.2% (Heim, et al. 2014). Most frequent mechanism of injuries was traffic accidents and falls from height. Blunt trauma accounted for 91.2% of the cases. A study by Nijboer et al. from Netherlands showed overall severe trauma mortality of 25% (Nijboer, et al. 2007). Other study from Bologna region in Italy noted 17.2% rate of severe trauma mortality with significant decrease in time being 25.8% in 1996 and 10.3% in 2004 (DiSaverio, et al. 2014). TBI accounted for most of the deaths at 58.4% followed by hemorrhage at 28.4%. Blunt trauma occurred in 97.1% of patients. A study based on the Germany trauma registry DGU reported 19.7% mortality of severely injured patients in 2012 with a decrease of 4.3% compared to 24.0% mortality in 1993 (TraumaRegister DGU(®) 2014). Thus, the overall mortality of severely injured patient in the European setting is ranging between 17.2% and 26.2% (DiSaverio, et al. 2014, Heim, et al. 2014, Nijboer, et al. 2007, TraumaRegister DGU(®) 2014, Rauf, et al. 2019).

Mean age is reported to range between 41 and 46 years and is increasing in time (Heim, et al. 2014, TraumaRegister DGU(®) 2014, Nijboer, et al. 2007). Most of the patients are male constituting over 70% of the cases in most of the investigations (TraumaRegister DGU(®) 2014, Heim, et al. 2014).

2.3. Trauma Repositories

2.3.1. Overview

Trauma repositories are important tools for monitoring outcomes and demographics of injured patients with a possibility of extraction the data at any time point with large number of cases including many regions and hospitals (Moore ja Clark 2008). Thus, trauma registries permit to conduct large-scale studies with high number of variables with a relatively short accrual time and constitute an integral component of a developed trauma system. However, development and management of injury repositories require significant amount of investments, time, dedicated and motivated team, and data validation. There are gold standard trauma repositories globally and the following description is to provide baseline characteristics of the databases.

2.3.2. National Trauma Data Bank®

NTDB® is the largest trauma registry involving a wide network of the American and Canadian trauma centers (NTDB® 1997). The NTDB establishment was initiated already in 1989 and the first call for data insertion was in 1997 (The American College of Surgeons 2019). Per the recent annual report, the NTDB® contains more than eight million patient records accrued from 765 separate trauma facilities (The American College of Surgeons 2018). The existence of such large and mature database provides an opportunity to review and validate both common and rare injuries using a large population (Aiolfi, et al. 2017, Englum, et al. 2016). A significant number of scientific reports are continuously published using the database.

2.3.3. TraumaRegister DGU®

DGU® was founded in 1993 with most participating hospitals located in Germany and more than 270 000 patients are inserted since the foundation (TraumaRegister DGU® 1993). Also, Belgium, Luxembourg, Finland, Austria, Netherlands, Switzerland, Slovenia and United Arab Emirates are contributing to DGU®. Overall, 675 hospitals are participating (AUC 2018). About 20 articles with large number of cases are published in accredited journals based on the DGU database annually.

2.3.4. The Trauma Audit & Research Network (TARN)

The TARN is the United Kingdom national trauma registry with mandatory data upload from all major trauma centers (Racy, Al-Nammari ja Hing 2014). The TARN was established in 1989 and consists over 200 000 cases with about 10% being pediatric patients (National Institute for Health and Care Excellence (UK) 2016). Many important scientific reports in high impact journals are published utilizing the TARN registry (Edwards 2015). For example, a study by Patel et al. regarding head injuries published in the Lancet initiated improvements in the entire trauma system in the UK (Patel, et al. 2005).

2.3.5. The Helsinki University Hospital trauma registry

The nearest trauma center to Estonia with trauma registry is Helsinki University Hospital. HTR was established in 2005 and covers Southern Finland with an estimated population of two million inhabitants. The first benchmarking study for the HTR was published in 2008 with an outcome comparison with a sample population from the TARN database (Handolin, et al. 2008). 1635 and 15 269 patients from the HTR and the TARN database were included, respectively,

showing better survival in the Helsinki University Hospital. Other more recent study comparing severely injured patients of the HTR with the DGU[®] registry reported similar outcomes with SMR of 0.79 and 0.82 in Southern Finland and at German hospitals, respectively (Brinck, et al. 2015).

2.3.6. Estonian Trauma Repository

Estonian trauma repository was initiated in 2015 including all severely injured patients admitted to the NEMC, TCH or TUH. The repository serves a population-based perspective as all the trauma centers in Estonia is involved. The first investigation published utilizing the data extracted from the repository is the Paper IV of the current thesis. A second recently published study about the role of elevated cardiac troponin on outcomes following severe chest trauma was partially using the repositories data (Keskpaik, et al. 2019). Thus, with a short period of time the repository has already contributed significantly showing the importance of registries as a part of trauma system.

2.3.7. Conclusion

Trauma repositories are highly important instruments in trauma systems allowing continuous data feedback with short accrual time including pooled data. The largest and most accredited registry globally is NTDB[®]. TARN and DGU[®] are the largest repositories in the European setting contributing many significant reports annually. HTR in Finland is an ideal registry for benchmarking against our trauma system as the Finnish demographics and trauma profile is similar to Estonia.

2.4. Autopsy studies

Majority of the trauma-related studies are conducted on patients admitted to health-care facilities, however, most of the injury related deaths occur in pre-hospital settings (Trunkey 1983). Thus, studies investigating population-based epidemiology of trauma deaths and injury-patterns are expected to include prehospital events and outcomes.

One of the most accredited and cited autopsy studies published by Shackford and colleagues in 1993 included all non-thermal injury related deaths in San Diego County during one-year period (Shackford, et al. 1993). Overall, 623 trauma victims were included in final analysis with most frequent cause of death being head injury at 40.3%, followed by hemorrhage at 30.5% and spinal cord injuries at 8.2% of the cases. Blunt and penetrating trauma accounted for 70.7% and 29.3% of the cases, respectively. Motor-vehicle accident was the pre-

dominant mechanism of injury constituting 55% of the deaths. Mean age was 36.4 years and 76.6% were male. Mean ISS was 49.7.

In the European region, a study from the Thames region in London analyzed a total of 434 trauma deaths (Daly ja Thomas 1992). Motor vehicle accidents were the most frequent mechanism of injury, 59% of the deaths occurred in a pre-hospital setting. Similarly, an investigation of 329 injury-related deaths in Diyarbakir city in Turkey also reported motor vehicle accidents as the most frequent mechanism of injury at 40% of the cases followed by falls from height at 33.7% (Yagmur, Kiraz ja Kara 1999). 69% were male. Another population-based study investigating traumatic deaths in Shanghai included 10,135 victims with a mean age was 40.9 years and males constituted 66%. Most frequent mechanism was traffic accidents (He, et al. 2015).

Hemorrhage is reported to be the second most common cause of death after head injuries with cardiac and aortic injuries predominating (Shackford, et al. 1993). An investigation including blunt trauma fatalities in the Los Angeles County found that 32% of the victims suffered cardiac injury with right atrium and right ventricle being the most frequently injured chamber at 30% and 27%, respectively (Teixeira, et al. 2009). A large study by Campbell et al. including 1,198 patients with penetrating cardiac injuries observed right ventricle as the most commonly injured cardiac chamber (Campbell , et al. 1997). A study by Shackelford et al. reported thoracic aortic injuries as the most frequent cause of death after train crash in Los Angeles County in 2011 (Shackelford, et al. 2011).

In summary, severe head injuries are the leading cause of death after injury (Shackford, et al. 1993), about two-third of trauma victims cases are males (Shackford, et al. 1993, Yagmur, Kiraz ja Kara 1999, He, et al. 2015, Sharma, et al. 2006) and the most frequent mechanism of injury is traffic accidents (Shackford, et al. 1993, Daly ja Thomas 1992, Yagmur, Kiraz ja Kara 1999). However, actual population-based studies with detailed analysis of exact injuries are scarce and most of the regional investigations are extrapolated to population-based estimates.

2.5. Summary of the Literature

The well-known classical trauma scores ISS, RTS and TRISS persist as the globally utilized standardized measures of injury severity.

Mortality of severely injured patients (ISS >15) is significantly decreased when admitted to a designated Level I trauma center.

Trauma repositories are important instruments in trauma systems allowing continuous data feedback with short accrual time and are integral part of modern trauma system.

Most of the trauma related deaths occur in a pre-hospital setting. Traffic accidents are reported as predominating mechanism of injury.

3. AIMS OF THE STUDY

The main purpose was to investigate demographics and outcomes of severely injured patients (ISS >15) in Estonia including comparison between Estonian trauma centers, between time periods of early and established independence, and with other trauma systems.

The specific aims were:

1. To study outcomes of severely injured patients comparing Estonian trauma centers NEMC+TCH versus TUH (Paper I).
2. To compare demographic patterns and outcomes of severe trauma during early vs. established independence of Estonia (Paper II).
3. To assess mechanism of trauma, injury profile and detailed causes of death of all injury-related fatalities after blunt or penetrating trauma in Estonia (Paper III).
4. To benchmark demographics, management and outcomes of severely injured patients of the NEMC against Helsinki University Hospital using regional trauma repositories (Paper IV).

4. MATERIAL AND METHODS

4.1. Inclusion and exclusion criteria (Papers I-IV)

4.1.1. Paper I

All consecutive trauma admissions with an ISS >15 to the NEMC+TCH and TUH between 1/1/2013 and 31/12/2013 were retrospectively reviewed. All age groups were involved.

4.1.2. Paper II

All adult patients (≥ 18 years) with an ISS >15 admitted to the NEMC or TUH between 1/1/1993 and 31/12/1994 versus 1/1/2013 and 31/12/2014 were retrospectively included.

4.1.3. Paper III

All consecutive autopsies after blunt or penetrating traumatic deaths between 1/1/2009 and 31/12/2013 (5-year period) were retrospectively included utilizing the National Forensic Medicine Database. Fatalities related to suffocation, freezing, burns or intoxication were excluded.

4.1.4. Paper IV

All severely injured (ISS >15) patients from the TTR and HTR were reviewed. Patients <16 years, patients with penetrating injuries and transfers from other hospitals were excluded (Figure 2).

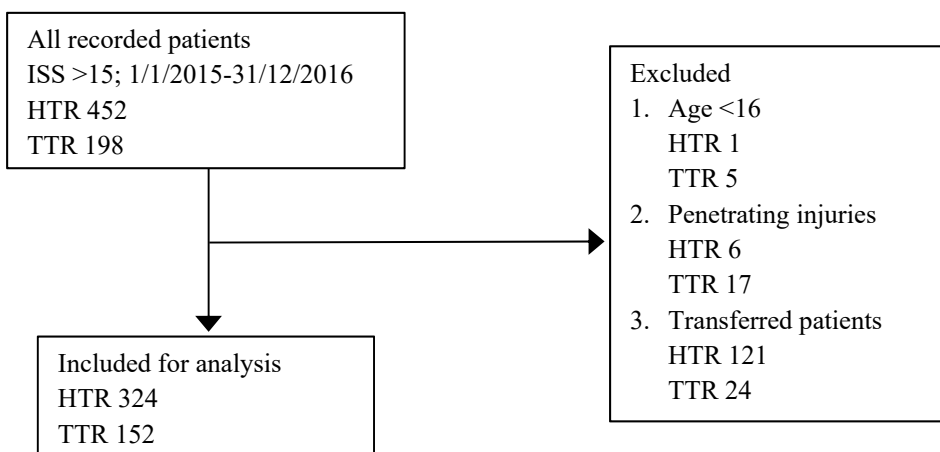


Figure 2. Flowchart of all included patients (Paper IV).

4.2. Data collection

Data collected included gender, age, mechanism of injury, vital signs, AIS-score, ISS, RTS, specific injuries, and cause of death (I–IV). TRISS score was calculated for the Paper I and IV. Data about complications per Clavien Dindo and HLOS were collected for the Paper I and II (Dindo, Demartines ja Clavien 2004).

Data for Paper IV was extracted from the prospective databases (HTR and TTR) with both repositories following the Utstein criteria. The TTR covers Northern Estonia with estimated population of 800 000 and was initiated in 2015. The HTR was established in 2005 and is covering Southern Finland comprising a population of 2 million inhabitants.

4.3. Statistical analysis

The p-values for categorical variables were derived from the Chi-square test or 2-sided Fisher's test (Papers I–IV). Student's *t* test or Mann-Whitney tests were utilized for continuous variables (Papers I–IV). P-value <0.05 was defined as statistically significant. Logistic regression analysis was used to compare defined outcomes adjusted for statistically significant (p-value <0.05) demographic variables and mechanism of injuries:

- complications, in-hospital mortality, HLOS, ICU-LOS (Paper I)
- complications, in-hospital mortality (Paper II)
- 30-day mortality (Paper IV)

Statistical analyses for Papers I–III were performed with the Statistical Package for Social Sciences (SPSS for Mac©), version 16.0 (SPSS Inc., Chicago, IL, USA) and for the Paper IV the R-program version 3.3.2 (R Foundation, Vienna, Austria) was utilized.

Values are reported as mean \pm standard deviation for continuous variables and as a percentage for categorical variables.

4.4. Outcomes

4.4.1. Paper I

Primary outcome was in-hospital mortality. Secondary outcomes included HLOS and complications per Clavien-Dindo. All the outcomes were compared between Estonian trauma centers (NEMC+TCH vs. TUH).

4.4.2. Paper II

Primary outcome was in-hospital mortality. Secondary outcomes were HLOS, complications per Clavien-Dindo, and incidence of penetrating trauma. All the outcomes were compared between the periods of early and established independence (1993–1994 vs. 2013–2014).

4.4.3. Paper III

Primary outcome was cause of death. Secondary outcomes were injury patterns.

4.4.4. Paper IV

Primary outcomes were 30-day mortality and SMR per the TRISS score. Secondary outcomes included HLOS and ICU-LOS.

5. RESULTS

5.1. Demographics and outcomes of severely injured patients in Estonia and comparison between trauma centers: North Estonia Medical Center + Tallinn Children's Hospital versus Tartu University Hospital (Paper I)

5.1.1. Demographics

Overall, 256 severely injured patients were admitted to the Estonian major trauma centers during the study period (1/2013–12/2013): 142 and 114 to the NEMC+TCH and TUH, respectively. Demographic profile is depicted in the Table 1. Patients admitted to the TUH were significantly older. Male patients predominated in both trauma centers. Overall, almost every second patient had a GCS below <9. Significantly higher proportion of cases was hypotensive on admission to the NEMC.

Most frequent mechanism of injury was ground level falls at 24.6% followed by non-ground level falls and auto versus pedestrian injuries constituting 19.6% and 10.5% of all admissions, respectively. Penetrating trauma accounted for 5.1% of cases (9.2% at the NEMC+TCH vs. 0% at the TUH, $p=0.003$).

Table 1. Demographic profile of all patients.

Characteristics	Overall n=256	NEMC+TCH n=142	TUH n=114	<i>p</i> -value
Age	47.2 ± 20.6	44.8 ± 21.4	50.3 ± 19.1	0.035
Age ≥ 65	18.4% (47)	17.6% (25)	19.3% (22)	0.728
Male	81.3% (208)	81.7% (116)	80.7% (92)	0.840
CCI	0.35 ± 0.89	0.37 ± 0.90	0.34 ± 0.92	0.810
GCS <9	44.1% (113)	46.5% (66)	41.2% (47)	0.400
SBP <90	13.3% (34)	18.3% (26)	7.0% (8)	0.008

5.1.2. Injury profile and severity

Injury scorings and profile are shown in the Table 2. Mean ISS was similar between the trauma centers. A number of critically injured patients (ISS >25) were significantly higher at the NEMC. Severe chest, abdominal and extremity injuries were more frequent at the NEMC, however, the rate of severe head injuries was higher at the TUH. Expected mortality per the TRISS score was higher at the NEMC without reaching statistical significance. A trend towards lower RTS score was noted at the NEMC ($p=0.161$).

TBI was the most frequent type of severe injury (Table 2) with SDH constituting vast majority of TBI subtypes (Table 3).

Table 2. Injury profile and scorings of all patients.

Characteristics	Overall n=256	NEMC+TCH n=142	TUH n=114	<i>p</i> -value
AIS head \geq 3	76.2% (195)	69.0% (98)	85.1% (97)	0.003
AIS thorax \geq 3	25.8% (66)	31.0% (44)	19.3% (22)	0.034
AIS abdomen \geq 3	10.9% (28)	14.8% (21)	6.1% (7)	0.028
AIS extremity \geq 3	13.7% (35)	18.3% (26)	7.9% (9)	0.016
ISS	23.6 \pm 7.8	23.7 \pm 9.1	23.5 \pm 6.1	0.835
ISS >25	18.0% (46)	23.2% (33)	11.4% (13)	0.014
RTS	6.2 \pm 1.8	6.0 \pm 1.8	6.3 \pm 1.7	0.161
TRISS	77.9 \pm 25.3	77.0 \pm 26.3	79.0 \pm 24.0	0.525
Expected mortality*	22.1%	23.0%	21.0%	0.789

*100%-TRISS

Table 3. TBI Subtypes

TBI Subtypes	Overall n=256	NEMC+TCH n=142	TUH n=114	<i>p</i> -value
EDH	11.7% (30)	11.3% (16)	12.3% (14)	0.802
SDH	59.8% (153)	50.0% (71)	71.9% (82)	<0.001
SAH	28.9% (74)	31.7% (45)	25.4% (29)	0.273
IVH	5.1% (13)	8.5% (12)	0.9% (1)	0.006
IPH	8.6% (22)	12.7% (18)	3.5% (4)	0.009

5.1.3. Surgical interventions

A total of 74.6% of the patients required surgery. Craniotomy was the most frequent surgical intervention performed in both centers (Table 4).

A total of 3.9% of the patients required interventional radiology (4.9% at the NEMC+TCH vs. 2.6% at the TUH, $p=0.519$).

Table 4. Surgical interventions

Surgical interventions	Overall n=256	NEMC+TCH n=142	TUH n=114	p-value
Surgery	74.6% (191)	75.4% (107)	73.7% (84)	0.761
Craniotomy/craniectomy	49.6% (127)	44.4% (63)	56.1% (64)	0.061
Laparotomy	6.6% (17)	8.5% (12)	4.4% (5)	0.194
Thoracotomy	2.3% (6)	2.8% (4)	1.8% (2)	0.695
Misscellaneous	16.0% (41)	19.7% (28)	11.4% (13)	0.071

5.1.4. Outcomes

The overall rate of complications was 40.2% and did not differ between the trauma centers (40.1% at the NEMC+TCH vs. 40.4% at the TUH, $p=0.973$). Grade II complications per Clavien-Dindo predominated with pneumonia being the most frequent adverse event.

Mean HLOS was 15.9 ± 20.7 days being significantly higher at the NEMC+TCH (20.1 ± 25.1 vs. 10.5 ± 11.2 days, $p<0.001$). ICU-LOS was 7.1 ± 10.6 and 4.4 ± 5.8 days at the NEMC+TCH and TUH, respectively ($p=0.019$). Overall ICU-LOS was 5.9 ± 8.9 days.

Overall mortality was 20.7%. Crude mortality was significantly higher at the NEMC+TCH (25.4% vs. 14.9%, $p=0.04$), however, adjusted mortality was similar in both trauma centers ($p=0.393$). Head injuries accounted for most of the deaths (Table 5).

Table 5. Mortality and Causes of Death

Characteristics	Overall n=256	NEMC+TCH n=142	TUH n=114	p-value
Crude mortality	20.7% (53)	25.4% (36)	14.9% (17)	0.040
*Adjusted mortality				0.393 (OR 1.38, CI 0.66–2.92)
Cerebral edema	73.6% (39/53)	66.7% (24/36)	88.2% (15/17)	0.180
Hemorrhage	15.1% (8/53)	16.7% (6/36)	11.8% (2/17)	1.00
Other causes of death	11.3% (6/53)	16.7% (6/36)	0% (0)	0.160

*adjusted for age, ISS> 25, SBP<90 mmHg, AIS head and neck/ thorax / abdomen/ extremity ≥ 3 , penetrating trauma, SDH, IVH, IPH

5.2. Evolution of severe trauma in Estonia comparing early versus established independence: 1993–1994 versus 2013–2014 (Paper II)

5.2.1. Demographics

A total of 1064 cases were included, 593 cases from the period of early independence (1993–1994) and 471 cases from the established independence period (2013–2014).

Demographics and injury profile is depicted in the Table 5. A mean age of patients admitted during the early independence period was significantly lower. Every fifth patient was hemodynamically unstable during admission between 1993–1994 being significantly higher compared to 13.0% during the established independence period ($p=0.001$). Prevalence of severe abdominal injuries was higher during early independence; however, severe extremity injuries were more frequent between 2013–2014.

Table 5. Demographics and Injury Profile of All Patients

Characteristics	1993–1994 n=593	2013–2014 n=471	<i>p</i> -value
Age	43.0 ± 15.3	53.2 ± 17.5	<0.001
Age > 65	7.8% (46)	25.1% (118)	<0.001
Male	85.8% (509)	78.1% (368)	0.001
SBP < 90 mmHg	20.4% (121)	13.0% (61)	0.001
GCS < 9	40.6% (241)	41.6% (196)	0.749
ISS	23.7 ± 8.8	23.3 ± 7.6	0.730
ISS > 25	19.7% (117)	16.6% (78)	0.184
AIS head ≥ 3	81.3% (482)	79.2% (373)	0.394
AIS thorax ≥ 3	20.2% (120)	21.7% (102)	0.571
AIS abdomen ≥ 3	17.4% (103)	11.0% (52)	0.004
AIS extremity ≥ 3	5.9% (35)	10.8% (51)	0.003

5.2.2. Mechanism of injuries

The rate of severe penetrating injuries was higher during the period of early independence (11.1% vs. 6.4%, $p=0.007$). The lower rate of penetrating trauma during the established independence period is mostly affected by significant decrease of gunshot wounds (Table 6). Also, prevalence of blunt assaults and motor vehicle crashes has decreased significantly (Table 6). The rate of ground level falls and bicycle crashes has increased in time (Table 6).

Table 6. Mechanism of injuries

Mechanism of injuries	1993–1994 n=593	2013–2014 n=471	<i>p</i>-value
Gunshot wounds	6.9% (41)	1.5% (7)	<0.001
Stab wounds	4.2% (25)	4.9% (23)	0.600
Ground level falls	20.1% (119)	46.5% (219)	<0.001
Non-ground level falls	13.2% (78)	16.1% (76)	0.170
Motor vehicle crashes	15.5% (92)	6.2% (29)	<0.001
Motorcycle crashes	2.7% (16)	1.9% (9)	0.400
Bicycle crashes	1.7% (10)	4.0% (19)	0.020
Auto vs. pedestrian	7.3% (43)	5.5% (26)	0.250
Struck by falling object	2.0% (12)	1.3% (6)	0.350
Hit, struck, kick by other person	14.7% (87)	7.4% (35)	<0.001
Other	11.8% (70)	4.7% (22)	<0.001

5.2.3. Surgical interventions

The overall surgical activity was similar between the periods with a trend towards higher rate of operations during the early period (76.9% vs. 72.2%, $p=0.079$). The number of laparotomies was significantly higher during the early period (13.7% vs. 7.9%, $p=0.003$). The rate of thoracotomies (2.5% in the early period vs. 2.8% in the established period, $p=0.815$), craniotomies (53.0% in the early period vs. 50.7% in the established period, $p=0.474$) and other surgical procedures were similar.

5.2.4. Specific injuries

All the specific injuries are shown in the Table 7. There were no IVC-injuries during the established period compared to 12 cases in the early period. SDH and SAH rate was significantly higher during the established period, however, IPH and IVH rate was higher in the early period. Overall, only one esophageal injury was diagnosed between 2013–2014.

Table 7. Specific Injuries of all patients

Characteristics	1993–1994 n=593	2013–2014 n=471	<i>p</i> -value
Traumatic brain injury			
EDH	14.5% (86)	12.3% (58)	0.300
SDH	41.3% (245)	63.3% (298)	< 0.001
IPH	16.7% (99)	10.6% (50)	0.005
SAH	14.8% (88)	25.1% (118)	< 0.001
IVH	8.8% (52)	4.7% (22)	0.009
Cardiac injuries	1.9% (11)	1.1% (5)	0.291
Lung injuries	7.9% (47)	10.4% (49)	0.161
Tracheal injuries	0.7% (4)	0	0.096
Esophageal injuries	0	0.2% (1)	0.443
Aortic injuries	1.9% (11)	1.1% (5)	0.291
Vena cava injuries	2.0% (12)	0	0.002
Diaphragmatic injuries	1.7% (10)	1.3% (6)	0.583
Liver injuries	6.9% (41)	4.7% (22)	0.124
Splenic injuries	5.1% (30)	4.7% (22)	0.771
Renal injuries	3.2% (19)	2.6% (12)	0.527

5.2.5. Outcomes

Overall complication rate was 42.2% and 35.2% during the early and established period, respectively ($p=0.022$). HLOS was similar between the periods (15.4 ± 19.0 vs. 15.7 ± 20.9 days, $p=0.920$).

Crude and adjusted mortality was significantly higher during the early period (Table 8). Every second patient admitted during the early period deceased with crude mortality rate of 50.3%. Most common cause of death in both periods was TBI.

Table 8. Crude and adjusted mortality and causes of death.

Characteristics	1993–1994 n=593	2013–2014 n=471	p-value	OR (95% CI)
Crude mortality	50.3% (298)	16.4% (77)	<0.001	
*Adjusted Mortality			<0.001	7.01 (4.69–10.47)
TBI	61.7% (184/298)	80.5% (62/77)	0.002	
Hemorrhage	15.4% (46/298)	7.8% (6/77)	0.080	
Septic complications	18.1% (54/298)	9.1% (7/77)	0.056	
Other	4.7% (14/298)	2.6% (2/77)	0.420	

*Adjusted for age, gender, hypotension on admission (SBP <90mmHg), AIS \geq 3 for abdomen and extremity, mechanism of injuries, laparotomy, different TBI subtypes, and vena cava injuries

5.3. Population-based autopsy study of traumatic fatalities (Paper III)

5.3.1. Demographics

During the 5-year study period, 1344 cases were included. Blunt and penetrating injuries constituted 75.7% and 24.3% of autopsies, respectively. Pre-hospital and in-hospital deaths accounted for 71.8% and 28.2% of the cases, respectively ($p < 0.05$). All the demographic data is represented in the Table 9. Most of the traumatic deaths were related to male patients being significantly higher in the penetrating trauma subgroup ($p=0.002$). Overall, more than half of the victims had a positive blood alcohol level (51.1%) and almost every tenth patient resulted positive at drug screening (8.3%).

Table 9. Demographics of all cases.

Characteristics	Total n=1344 100.0%	Blunt n=1018 75.7%	Penetrating n=326 24.3%	p-value
Age	50.4 \pm 18.5	51.0 \pm 19.2	48.5 \pm 16.0	0.034
Age >65	22.1%	24.5%	14.7%	<0.001
Age <18	2.4%	3.0%	0.6%	0.016
Male	77.1%	75.0%	83.4%	0.002
Accident	64.4%	83.7%	4.0%	<0.001
Assault	20.5%	10.6%	51.2%	<0.001
Suicide	15.2%	5.7%	44.8%	<0.001
Blood alcohol level +	51.1%	47.2%	61.2%	<0.001
Drugs +	8.3%	8.5%	7.8%	0.874

5.3.2. Mechanism of injuries

Most frequent mechanism of injury was motor vehicle accident constituting 18.7% of all deaths followed by non-ground level falls and ground level falls at 14.7 and 14.0%, respectively (Table 10).

Table 10. Mechanism of injury.

Mechanism of injury	Overall n = 1344 (100.0%)
Motor vehicle accident	18.7%
Non-ground level fall	14.7%
Ground level fall	14.0%
Sharp object	13.1%
Gunshot wound	11.2%
Auto vs. Pedestrian	11.1%
Hit, struck or kick by other person	8.0%
Bicycle accident	3.0%
Motorcycle accident	1.5%
Other or unknown	4.7%

5.3.3. Abbreviated Injury Scale and Injury Severity Score

Overall mean ISS was 39.7 and significantly higher in the penetrating trauma group at 47.7 ($p < 0.001$). A total of three out of four patients had a severe head injury and almost half of the patients had severe chest injuries (Table 11).

Table 11. ISS and AIS of all autopsies.

Characteristics	Total n=1344 100.0%	Blunt n=1018 75.7%	Penetrating n=326 24.3%	p-value
ISS	39.7 ± 23.9	37.1 ± 22.0	47.7 ± 27.8	<0.001
AIS head/neck ≥3	74.9%	82.2%	51.8%	<0.001
AIS chest ≥3	46.4%	48.3%	40.2%	0.010
AIS abdomen ≥3	24.5%	27.3%	15.6%	<0.001
AIS extremity ≥3	19.9%	24.0%	7.4%	<0.001

5.3.4. Primary outcome: Causes of death

Most frequent cause of death was head injury at 50.5% followed by hemorrhage and multiple lethal injuries constituting 30.4% and 10.9% of all deaths. Other less frequent causes were cardiopulmonary failure (4.4%), spinal cord injury (2.2%) and sepsis/ multi-organ failure/ pneumonia (1.6%) (Figure 3).

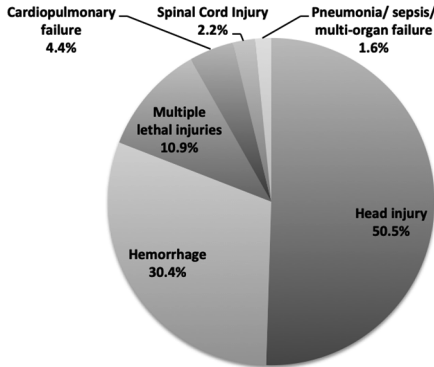


Figure 3. Causes of death.

5.3.5. Secondary outcome: Injury patterns

A total of 29.4% of the patients had a skull fracture. Most frequent type of intracranial bleeding was SAH at 44.5% followed by SDH (27.8%) and IVH (10.6%).

Overall, 10.9% (n=147) and 10.9% of the patients had cardiac injuries and aortic injuries, respectively. The most frequently injured chamber was right ventricle followed by left ventricle (Figure 4).

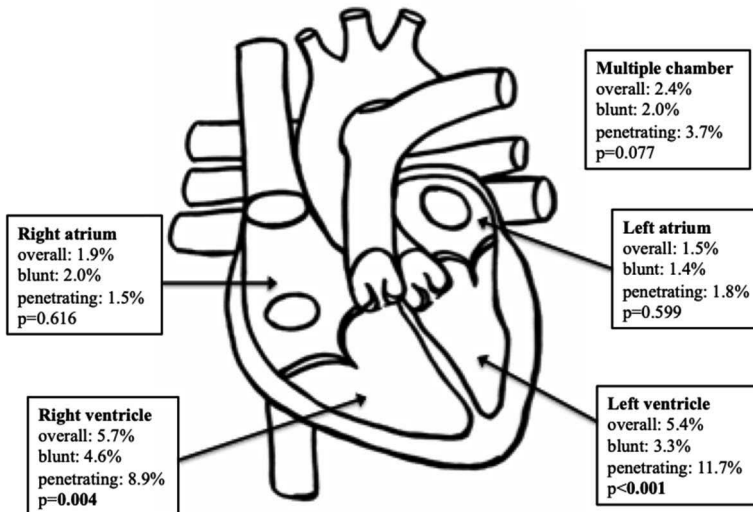


Figure 4. Cardiac injuries.

Most frequent intra-abdominal solid organ injury was liver injury at 21.7%. Splenic and renal injuries were encountered at 12.3 and 6.4% of the cases, respectively.

5.4. Severe blunt trauma in Finland and Estonia: comparison of two regional trauma repositories

5.4.1. Demographic profile

All the demographic profile is showed in the Table 12. No statistically significant differences were noted. A high proportion of patients older than 65 years are admitted in both institutions.

Table 12. Demographic profile of all patients.

Characteristics	TTR n=152	HTR n=324	p-value
Age (years)	47.7 ± 19.2	48.4 ± 20.1	0.694
Age >65 years	19.7% (30)	23.5% (76)	0.429
Male	73.7% (112)	72.5% (235)	0.878
GCS < 9	28.3% (43)	33.6% (109)	0.288
SBP < 90 mmHg	12.5% (19)	9.0% (29)	0.300

5.4.2. Abbreviated Injury Scale and Injury Severity Score

Mean ISS was similar in both regions (p=0.678). Significantly higher proportion of patients with severe abdominal injuries was admitted in Northern Estonia compared to Southern Finland (p=0.002). A trend towards higher rate of severe chest injuries in Southern Finland was noted (p=0.112) (Table 13).

Table 13. ISS and AIS of all patients.

Characteristics	TTR n=152	HTR n=324	p-value
ISS	25.7 ± 10.1	26.1 ± 9.7	0.678
AIS head ≥ 3	56.6% (86)	61.4% (199)	0.366
AIS chest ≥ 3	52.0% (79)	60.2% (195)	0.112
AIS abdomen ≥ 3	25.0% (38)	13.3% (43)	0.002
AIS extremity ≥ 3	27.6% (42)	31.5% (102)	0.456

5.4.3. Mechanism of injuries

Non-ground level fall was predominant mechanism of injury in both regions followed by motor vehicle accidents. The rate of non-ground level falls is significantly higher in the Northern Estonia ($p=0.046$). Patients injured in bicycle accidents are more frequent in the Southern Finland region ($p=0.008$).

Table 14. Mechanism of injuries.

Mechanism of injuries	TTR n=152	HTR n=324	<i>p</i> -value
Non-ground level fall	32.9% (50)	23.8% (77)	0.046
Motor vehicle accident	17.1% (26)	15.1% (49)	0.676
Ground level fall	11.8% (18)	15.1% (49)	0.413
Auto vs. pedestrian	11.2% (17)	5.9% (19)	0.063
Motorcycle accident	8.6% (13)	12.0% (39)	0.328
Bicycle accident	3.9% (6)	12.0% (39)	0.008
Other or unknown	14.5% (22)	16.0% (52)	0.759

5.4.4. Outcomes

Mean HLOS was 26.3 ± 36.1 and 12.4 ± 10.3 in TTR and HTR, respectively ($p=0.003$). Mean ICU-LOS was 14.3 ± 17.5 and 8.5 ± 7.3 in TTR and HTR, respectively ($p=0.044$), however, ventilation days were similar (10.7 ± 15.3 in TTR vs. 6.6 ± 6.3 in HTR, $p=0.288$).

Primary outcomes are represented in the Table 15. Crude and adjusted mortality were similar between the regions. Both hospitals showed lower mortality compared to expected mortality per TRISS.

Step-down hospital as a discharge destination was more frequently utilized at the Helsinki University Hospital (58.0% vs. 18.1%, $p<0.001$), however, home more frequently at the NEMC (50.7% vs. 20.7%, $p<0.001$). Also, a higher rate of patients was discharged to rehabilitation from the NEMC (16.4% vs. 6.2%, $p<0.001$).

Table 15. TRISS, SMR and 30-day mortality of all patients.

Characteristics	TTR n=152	HTR n=324	p-value
TRISS	81.1 ± 26.2	79.2 ± 25.5	
Expected mortality ^a	18.9%	20.8%	
30-day in-hospital crude mortality	14.5%	13.6%	0.904
30-day adjusted mortality ^b			0.762
Difference ^c (SMR ^d)	-4.4% (0.77)	-7.2% (0.65)	>0.05

^a100.0%-TRISS

^badjusted for AIS abdomen ≥ 3, bicycle accident, non-ground level falls

^c30-day crude (observed) mortality-Expected mortality

^d30-day crude (observed) mortality/Expected mortality

6. DISCUSSION

Severe injuries are significant public health concern globally and in Estonia constituting high proportion of all causes of death and morbidity. Nevertheless, studies focusing on severe trauma in Estonia are scarce. Thus, the current thesis investigates comprehensively severe injuries in Estonia including different time segments, trauma centers, pre- and in-hospital trauma deaths and comparisons with other trauma systems.

The first study investigating severely injured patients admitted between 1/2013 and 12/2013 to the Estonian trauma centers found overall crude mortality of 20.7% being similar to other European trauma centers reporting overall mortality ranging from 17.2% to 26.2% (DiSaverio, et al. 2014, Nijboer, et al. 2007, TraumaRegister DGU(®) 2014, Rauf, et al. 2019) (Paper I). However, a study including 45 Level I trauma centers in USA reported overall mortality of 14.9% for severely injured patients being lower compared to Estonian and European settings (Demetriades, et al. 2006). Thus, the mortality was acceptable in 2013, however, with significant potential for improvements.

Nevertheless, the overall in-hospital mortality during the early independence period was devastating being 50.3% between 1993 and 1994 showing notable improvements in the management of trauma patients during the following decades (Paper II). Also, other regions in Europe have noted decreased mortality of severely injured patients in time, however, not so drastically. The largest trauma registry in the European region DGU[®] reported 4.3% decrease of mortality from 24.0% in 1993 to 19.7% in 2012 (TraumaRegister DGU(®) 2014).

A very high mortality during nineties is certainly multifactorial and may reflect a poor state of trauma system at that time in Estonia. Advancements in pre-hospital care and system, introduction of damage control resuscitation and surgery, trauma team activation criteria, evidence-based guidelines and management, better medical equipment, prompt availability and accessibility of radiological investigations, evolved surgical critical care and rehabilitation have all contributed to the evolution of management of severely injured patients with significantly improved outcomes.

Nevertheless, as previously mentioned, a room for improvements existed. The ATLS course as a baseline “Gold Standard” trauma course was introduced in 2015 (American College of Surgeons 1980). Also, an active research involving trauma patients was initiated and since 2015 a prospective trauma repository exists in Estonia. A study extracting data from trauma repositories comparing outcomes of severely injured patients admitted to the NEMC versus to the Helsinki University Hospital between 1/2015 and 12/2016 showed similar crude and adjusted mortality in both regions (Paper IV). Overall 30-day mortality at the NEMC was 14.5% being significantly lower compared to the expected mortality per TRISS methodology (Paper IV). Thus, it is prudent to speculate that the improved outcomes may be result of recent reforms and developments within the Estonian trauma system. Also, as demographic profile in Finland is very similar

to Estonia it is an ideal population for comparison and benchmarking. Thus, since Estonia regained independence in 1991, the evolution of the trauma system has been remarkable with improved trauma outcomes involving very different periods of time and confirming that the system is evolving significantly.

The Estonian trauma centers showed similar adjusted primary outcomes (Paper I). The NEMC admitted significantly higher rate of patients with unstable hemodynamics (SBP <90mmHg), with severe chest, abdominal and extremity injuries and critical injury burden (ISS >25) explaining the higher crude mortality. However, after adjustment, the mortality did not differ between the major Estonian trauma facilities ($p=0.393$). Thus, the NEMC cares for higher rate of complex and critical patients. The higher proportion of critically injured patients also explains significantly longer HLOS at the NEMC. Head injuries were the primary cause of death in both trauma centers.

Blunt trauma accounts for 91.2 to 97.1% of all severe trauma cases reported by different European institutes (Heim, et al. 2014, DiSaverio, et al. 2014, TraumaRegister DGU(®) 2014). Demographic profile in Estonia is typical for European setting with blunt injuries predominating. Non-ground level falls was the predominating mechanism between 1/2015 and 1/2016 similarly to Finland constituting almost third of all the injury mechanism (Paper IV). Ground level falls was the most frequent mechanism of injury in 2013 followed by non-ground level falls (Paper I). Overall severe penetrating trauma rate have been below 10% in recent years (Paper I, II). Nevertheless, penetrating trauma mechanisms were significantly higher during nineties constituting 11.1% of all severe trauma cases, being remarkably high for an European setting (Paper II), thus, being similar to USA trauma population reporting 11.2% of severe penetrating trauma admissions (Demetriades, et al. 2006). Lack of effective gun control, fragmented law-enforcement capabilities, relatively low overall income, high rate of organized crime and interpersonal violence were all contributing to the high rate of penetrating trauma in Estonia during nineties. The National Institute for Health Development reported 27.6 homicides per 100 000 in Estonia between 1993–1994, thus, if the violent death rate would be similar at the present time Estonia would be in the top 20 of most violent countries in the world (UNODC Statistics Online 2018, The National Institute of Health Development 2015). Fortunately, the interpersonal violence and criminal activity has decreased significantly with homicide rate of 2.2 per 100 000 in 2017 placing Estonia to the 140th position between all the countries (UNODC Statistics Online 2018). A significantly lower rate of gunshot wounds has the highest impact for overall decrease of penetrating injuries (Paper II). Possible causes are overall economic improvement, strict gun-control legislation and improved law-enforcement capabilities (Riigi Teataja 2001). Thus, even with a high trauma caseload during nineties, injury outcomes were detrimental due to a lack of proper trauma system and non-existing continuous trauma education.

The population-based autopsy study including all traumatic deaths after penetrating or blunt injuries in Estonia is a pioneering study involving the entire Estonian population instead of extrapolating to population-based estimates

(Paper III). Also, autopsy studies include pre-hospital deaths offering information about cases, which are usually excluded in most studies and involving in-hospital deaths only. Our study showed that more than two third of deaths occurred in a pre-hospital setting, thus, proving again that with effective injury prevention, many lives could have been saved.

Similar to other reports, MVA was the most frequent cause of death in Estonia (Shackford, et al. 1993, Daly ja Thomas 1992, Yagmur, Kiraz ja Kara 1999). Traffic accidents are among top ten leading causes of death in the world per the recent WHO report and with possible increase during next decades (WHO 2008).

Highly disturbing notion was in our study that more than half of the trauma victims had a positive blood alcohol level at the time of death and the rate was even higher in victims succumbing in penetrating injuries (Paper III). Estonian public alcohol-prevention measures have been more or less aggressive in recent years with raised excise duty on alcohol, time restrictions for alcohol sale, frequent alcohol breath tests for drivers, strict rules for alcohol advertisement and national campaigns about alcohol harm resulting in a lowest alcohol consumption per person during last decade in 2019 (National Institute for Health Development 2019, Ministry of Social Affairs 2019). Nevertheless, alcohol abuse is still a significant problem in Estonia and active continuous national initiative for alcohol harm-reduction is of paramount important in Estonian society.

Overall, head injuries were the leading cause of death constituting 50.5% of all cases followed by hemorrhage at 30.4% (Paper III). A study by Shackford et al. reported similar results with head injuries and hemorrhage related deaths constituting 40.3% and 30.5% of all cases, respectively (Shackford, et al. 1993). Thus, head injuries are the predominant cause of death in both pre-hospital and in-hospital setting irrespective of the region.

A large proportion of patients (10.9%) had a cardiac injury at the moment of death with a right ventricle being the most frequently injured chamber overall (Paper III). Thus, if we include deceased patients only the number of cardiac injuries is surprisingly high. A large study by Teixeira and colleagues found that right cardiac chambers were the most frequently injured after blunt trauma with right atrium being most frequently injured followed by right ventricle (Teixeira, et al. 2009). However, in our study right ventricle was the most frequently injured chamber followed by left ventricle after blunt trauma. In a study by Campbell et al. right ventricle injuries were most frequent followed by left ventricle after penetrating trauma (Campbell , et al. 1997). Left ventricle was the most frequently injured chamber in our study followed by right ventricle in case of penetrating trauma.

The limitations of the current thesis include retrospective nature of the publications I–III and rather low number of patients in the publications I and IV. Nevertheless, these are very first studies investigating comprehensively severely injured patients in Estonia with evolving trauma system. The studies showed comprehensively the overall evolution and state of Estonian trauma system with very important input for future improvements.

7. CONCLUSIONS

1. Outcomes of severely injured patients were similar between the Estonian trauma centers.
2. Estonian trauma system has evolved significantly from early independence to established independence.
3. Head injuries were the predominating cause of death in the pre-hospital and in-hospital setting followed by hemorrhage related deaths.
4. Most of the injury related deaths occurred in a pre-hospital setting showing the importance of prevention.
5. MVA was the leading mechanism of injury after traumatic deaths.
6. High rate of patients with positive BAL after traumatic deaths warrants continuous national preventive measures.
7. The benchmarking study comparing outcomes of severely injured patients with the Helsinki University Hospital showed similar adjusted mortality.

8. SUMMARY IN ESTONIAN

Raske trauma epidemioloogia Eestis

8.1. Sissejuhatus

Vigastussurmade tõttu kaotatud eluaastate hulk on suurem kui kasvajate ja südamehaiguste tõttu kaotatud eluaastate hulk kokku (Trunkey 1983). WHO andmetel hukub trauma tõttu maailmas keegi iga kuue sekundi järel (WHO 2015). Vigastussurmade osakaal Eestis on üks Euroopa Liidu kõrgemaid (EuroSafe 2013, EuroSafe 2014, EuroSafe 2016). Seega on traumaatilised vigastused märkimisväärne probleem nii globaalselt kui regionaalselt Eestis.

Raske trauma on defineeritud kui ISS >15 ja on näidatud, et sellise vigastuskoormusega patsientide elulemus on oluliselt parem, kui suunamine on koheselt kõrgema astme traumakeskusesse, mida Eestis esindavad Põhja-Eesti Regionaalhaigla (PERH) ja Tartu Ülikooli Kliinikum (TÜK) (Demetriades, et al. 2006, Baker, et al. 1974). Eestis puudusid varasemalt raskele traumale fookuseeritud uuringud ning antud käsikirja eesmärgiks on põhjalikult uurida antud haigete demograafilisi andmeid ja tulemeid Eestis.

8.2. Eesmärgid

Peamiseks eesmärgiks oli hinnata raskelt vigastatute (ISS >15) demograafiat ja käsitluse tulemeid Eestis. Täpsemad eesmärgid olid:

1. Võrrelda raskelt vigastatute tulemeid PERH-i ja TÜK-i vahel.
2. Võrrelda raskelt vigastatud haigete demograafiat ja tulemeid erinevatel ajaperioodidel (1993–1994 vs. 2013–2014) taasiseseisvunud Eestis.
3. Hinnata traumamehhanisme, vigastusmustreid ja täpseid surmapõhjuseid kõikidel tõmbi või penetreeriva trauma tõttu hukkunutel.
4. Võrrelda raskelt vigastatute tulemeid PERH-is, Eesti suurimas traumakeskuses, Helsingi Ülikooli haigla traumakeskusega.

8.3. Uuritavad ja meetodid

Esimesse uuringusse kaasati retrospektiivselt kõik raske traumaga (ISS >15) patsiendid, kes hospitaliseeriti PERH-i ja Tallinna Lastehaiglas (TLH) või TÜK-i ajavahemikul 1/1/2013 kuni 31/12/2013.

Teise uuringusse kaasati retrospektiivselt kõik raskelt vigastatud haiged, kes hospitaliseeriti TÜK-i või PERH-i ajavahemikul 1/1/1993–31/12/1994 (varane periood) ja 1/1/2013–31/12/2014 (hilisem periood).

Kolmandasse uuringusse kaasati retrospektiivselt kõik tõmbi või läbiva vigastuse tõttu surnud patsiendid Eestis ajavahemikul 1/1/2009 kuni 31/12/2013, kasutades kõigi nelja Eesti kohtuarstliku keskuse lahanguandmeid.

Neljandas uuringus võrreldi PERH-i traumakogumi ja Helsingi Ülikooli haigla traumakogumi alusel raskelt vigastatud (ISS >15) haigete tulemeid.

Statistilisel analüüsimisel kasutati pidevate andmete võrdlemisel *Student t-test*-i või Mann-Whitney testi ja kategoriseeritavate andmete võrdlemisel kasutati hii-ruut testi või Fischer'i testi. Kohandatud tulemite võrdlemisel rakendati vajadusel logistilist regressioon analüüsi.

8.4. Tulemused

Esimesse uuringusse kaasati 256 vigastatud üldsuresusega 20.7%. Peamine surmapõhjus oli ajuvigastus. Kohandatud suremus oli traumakeskuste vahel sarnane (*adj. p*=0.393). Haiglas viibimise aeg oli PERH-is oluliselt pikem, mis on ilmselt mõjutatud suuremast hulgast kriitiliselt vigastatud haigetest PERH-is.

Teise uuringusse kaasati 1064 patsienti, 593 patsienti varasest perioodist ja 471 hilisemast perioodist. Oluliselt on vähenenud penetreerivate vigastuste hulk ja seda eelkõige laskevigastuste arvelt. Komplikatsioonide hulk haiglasoleku ajal oli varases perioodis oluliselt kõrgem (42.2% vs. 35.2%, *p*= 0.022). Drastiliselt on vähenenud raskelt vigastatute suremus, mis oli varases perioodis 50.3% ja 16.4% hilisemas perioodis (*adj. p*<0.001). Mõlemas perioodis oli peamine surmapõhjus ajuvigastus.

Kolmas uuring kaasas 1344 tõmbi või läbiva vigastuse tõttu surnut. Tõmbid ja läbivad vigastused moodustasid vastavalt 75.7% ja 24.3%. Enamus surmadest toimus haiglaeelselt (71.8%). Peamine mehhanism oli autoõnnetus. Surma hetkel esines alkoholijoove 51.1%-l hukkunutest. Peamine surmapõhjus oli peavigastus, moodustades 50.5% surmadest, millele järgnes veritsussurm 30.4%-ga.

Neljas uuring kaasas 152 juhtu PERH-ist ja 324 juhtu Helsingi Ülikooli haiglast. Demograafiline profiil oli haiglate vahel suhteliselt sarnane. Nii üldsuresumus kui kohandatud suremus oli haiglate vahel sarnane. Mõlemad haiglad näitasid paremaid tulemeid, kui oli oodatav suremus TRISS alusel.

8.5. Järeldused

1. Eesti traumakeskuste tulemid raskelt vigastatud haigete käsitlemisel olid sarnased.
2. Raske traumaga haigete suremus on ajas oluliselt langenud.
3. Peamine surmapõhjus oli ajuvigastus nii haiglaeelselt kui haiglas surnutel.
4. Mootorsõiduki õnnetus oli peamine mehhanism vigastussurma korral.
5. Enamus vigastussurmasid toimus haiglaeelses etapis.
6. Väga suurel hulgal (51%) vigastustesse surnutel esines alkoholijoove.
7. PERH-i kui Eesti suurima traumakeskuse tulemid olid sarnased Helsingi Ülikooli haiglaga.

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Major trauma related projects

Development and management of *Estonian Trauma Repository*. Since 2015.

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1. Trauma Evaluation and Management (TEAM) for students. Tartu, Estonia, 2019 (as an instructor)
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8. **GlobalSurg Collaborative.** Surgical site infection after gastro-intestinal surgery in high-income, middle-income and low-income countries: a prospective, international, multicentre cohort study. *Lancet Infect Dis.* 2018;18(5):516–525.
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Non Peer Reviewed

1. **Saar S**, Lepp J, Laar P, Jaanson T, Lipping E, Talving P. Left-sided paraduodenal hernia: review of the literature and a case report. *Eesti Arst*. In press.
2. **Saar S**, Lepp J, Popov A, Novak V, Lepner U, Asser T, Rätsep I, Väli M, Starkopf J, Talving P. Trauma system and outcomes of severely injured patients in Estonia. *Eesti Arst*. 2018;97(11):623–627.
3. **Saar S**, Laars M, Graumann K, Väli M, Ilmoja ML, Rimmelgas A, Lepner U, Starkopf J, Talving P. Pedestrian injuries caused by traffic accidents in Estonia: analysis of 116 consecutive cases from regional hospitals and autopsy reports from forensic science institutions. *Eesti Arst*. 2017;96(11):655–660.
4. Talving P, Mihnovitš V, Lepner U, **Saar S**. Contemporary Management of Acute Appendicitis. *Eesti Arst*. 2016;95(11):723–727. (Best article of the North Estonia Medical Centre, 2016)
5. Talving P, Ilmoja ML, Taal G, Isand KG, Teppo S, Noor EH, Kruusat R, Rimmelgas A, **Saar S**. Blunt Cardiac Rupture in a Toddler. *Journal of Pediatric Surgery Case Reports*. 2016;11:1–3.
6. Talving P, **Saar S**, Lam L. Management of Penetrating Trauma to the Major Abdominal Vessels. *Curr Trauma Rep*. 2016;2:21–8.
7. Nikkolo C, **Saar S**, Sokirjanski M, Junkin LK, Lepner U. Retrospective Study of Surgical Treatment of Primary Hyperparathyroidism at Tartu University Hospital. *Eesti Arst*. 2014;93(11):622–626.

Oral presentations at international congresses

1. **Saar S**, Mihnovitš V, Lustenberger T, Rauk ML, Noor EH, Lipping E, Lomp A, Isand KG, Lepner U, Talving P. Twenty-four hour versus Extended Antibiotic Administration After Surgery in Complicated Appendicitis: A Randomized Controlled Trial. 77th Annual Meeting of the American Association for the Surgery of Trauma, San Diego, USA, Sept 26–29, 2018.

2. **Saar S**, Laos J, Ilmoja ML, Metsvaht T, Laasma M, Märtson M, Sokirjanski M, Varik K, Talving P. Population-based Pediatric Trauma in Estonia: Forty-eight Consecutive Cases Analyzed. XIV Conference of The Baltic Association of Paediatric Surgery, Estonia, Tartu, May 7, 2016.
3. **Saar S**, Sokirjanski M, Junkin LK, Laos J, Laar AL, Merioja I, Lepner U, Kukk L, Remmelgas A, Asser T, Innos K, Starkopf J, Talving P. Evolution of Severe Trauma in Estonia Comparing Time Segments of Early versus Established Independence of the State. 17th European Congress of Trauma & Emergency Surgery, Vienna, Austria. April 26, 2016.
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5. **Saar S**, Sokirjanski M, Junkin LK, Laos J, Laar AL, Merioja I, Lepner U, Asser T, Ilmoja ML, Kukk L, Remmelgas A, Talving P. Severe Trauma in Estonia: 254 consecutive cases analysed. 8th Congress of The Baltic Association of Surgeons, Tallinn, Estonia. September 10–12, 2015.

Poster presentations at international congresses

1. **Saar S**, Reinsoo A, Talving P, Vanakesa T, Saluvere P, Almre I. Esophageal perforations at a referral medical facility: a 17-years perspective. 19th European Congress of Trauma & Emergency Surgery, Valencia, Spain, May 6–8, 2018.
2. Mohseni S, Ivarsson J, Ahl R, Dogan S, **Saar S**, Reinsoo A, Sepp T, Isand KG, Garder E, Kaur I, Ruus H, Talving P. Simultaneous laparoscopic cholecystectomy and intra-operative ERCP for common bile duct stones: Experience of the one-step approach at two referral hospitals. 76th Annual Meeting of AAST and Clinical Congress of Acute Care Surgery, Baltimore, USA, Sept 13–16, 2017.
3. **Saar S**, Lepner U, Laos J, Sokirjanski M, Lustenberger T, Mihnovitš V, Lomp A, Talving P. Performance of Diagnostic Modalities in Acute Appendicitis. 47th World Congress of Surgery, Switzerland, Basel, Aug 13–17, 2017.
4. Mihnovitš V, **Saar S**, Lomp A, Rajas M, Reinsoo A, Ilves P, Lepner U, Talving P. Risk of Malignancy in Patients with Appendiceal Mass. 47th World Congress of Surgery, Switzerland, Basel, Aug 13–17, 2017.
5. Lomp A, Mihnovitš V, **Saar S**, Ilves P, Reim M, Väli M, Talving P, Lepner U. One Hundred and Five Consecutive Liver Injuries Analysed: an Estonian Experience. 18th European Congress of Trauma & Emergency Surgery, Bucharest, Romania, May 7–9, 2017.
6. Einberg M, **Saar S**, Seljanko A, Lomp A, Ruusalepp A, Vanakesa T, Laisaar T, Taal G, Talving P. A 23-years Perspective of Cardiac Injuries at Estonian Major Trauma Facilities. 18th European Congress of Trauma & Emergency Surgery, Bucharest, Romania, May 7–9, 2017.

7. Merioja I, **Saar S**, Laar AL, Laos J, Lomp A, Kontkar K, Seljuškin D, Soosaar I, Tõru T, Avi A, Asser A, Kukk L, Asser T, Starkopf J, Talving P. Population-based investigation on isolated severe traumatic brain injury severity and outcomes in Estonia. EANS 2016, Greece, Athens, September 4–8, 2016.
8. **Saar S**, Merioja I, Lustenberger T, Lepner U, Asser T, Metsvaht T, Ilmoja ML, Kukk L, Talving P. Severe Trauma in Estonia: 256 consecutive cases analysed and the impact on outcomes comparing two regions. 16th European Congress of Trauma & Emergency Surgery, Amsterdam, Netherlands. May 10–12, 2015.

Invited lectures at international congresses

1. *Severe traumatic brain injury: Estonian perspective*. 14th congress of Baltic Neurosurgical Association, Tartu, Estonia, May 25, 2018.
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Invited lectures at local congresses

1. *Non-operative Management of Penetrating Abdominal Trauma*. Clinic 2018. Tartu, Estonia. February 6, 2018.
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3. *Severe Trauma: Estonia vs. South Africa*. Autumn Congress of The North Estonia Medical Centre. Tallinn, Estonia. Oct 30, 2015.
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Haridus

Ülikool: Arstiteaduskond, Tartu Ülikool, Tartu, Eesti, 2009–2015.
Alg-, põhi- ja keskkool: Tallinna Reaalkool, Tallinn, Eesti, 1996–2008.

Fellowship

Kliiniline ja teaduslik *fellowship* Groote Schuur-i haiglas, Kaplinn, LAV, okt 2019–dets 2019.

Traumaga seotud suurprojektid

Raske trauma kogumi loomine Eestis. 2015.

Traumaalased kursused

1. *Trauma Evaluation and Management (TEAM) for students*. Tartu, Eesti, 2019 (instruktorina)
2. *Advanced Surgical Skills for Exposure in Trauma (ASSET)*. Tartu, Eesti, 2018 (osalejana)
3. *Definitive Surgical Trauma Care (DSTC)*. Tartu, Eesti, 2017 (osalejana)
4. *Advanced Trauma Life Support (ATLS)*. Tartu, Eesti, 2016 (osalejana)

Auhinnad

1. *Best International Abstract Award. 77th Annual Meeting of AAST*. San Diego, USA, sept 2018.
2. Parim artikkel Eesti Arstis. Tallinn, Eesti, 2016.

Stipendiumid

1. Andreas ja Elmerice Traksi stipendium, Tartu Ülikool, 2019.
2. Noore Arsti Stipendium, Põhja-Eesti Regionaalhaigla, 2019.
3. Hilda ja Harry Mägi stipendium, Tartu Ülikool, 2017.
4. Liisa Kolumbuse Mälestusfondi stipendium, Tartu Ülikool, 2016.

Publikatsioonid

Eelretsenseeritud

1. **GlobalSurg Collaborative.** Global variation in anastomosis and end colostomy formation following left-sided colorectal resection. *BJS Open.* 2019;28;3(3):403–414.
2. Keskpaiik T, Talving P, Kirsimägi Ü, Mihnovišt V, Lomp A, Raamat EM, **Saar S**, Starkopf J. The Role of Elevated High-sensitivity Cardiac Troponin on Outcomes Following Severe Blunt Chest Trauma. *Injury.* 2020. In press.
3. **GlobalSurg Collaborative.** Pooled analysis of WHO Surgical Safety Checklist use and mortality after emergency laparotomy. *Br J Surg.* 2019;106(2).
4. **Saar S**, Brinck T, Laos J, Handolin L, Talving P. Severe blunt trauma in Finland and Estonia: Comparison of two regional trauma repositories. *Eur J Trauma Emerg Surg.* 2019. In press.
5. **Saar S**, Mihnovišt V, Lustenberger T, Rauk ML, Noor EH, Lipping E, Isand KG, Lepp J, Lomp A, Lepner U, Talving P. Twenty-four hour versus extended antibiotic administration after surgery in complicated appendicitis: a randomized controlled trial. *J Trauma Acute Care Surg.* 2019;86(1):36–42 (*Featured article, January 2019*).
6. Einberg M, **Saar S**, Avrutina A, Lomp A, Lepner U, Talving P. Cardiac Injuries at Estonian Major Trauma Facilities: A 23-years Perspective. *Scand J Surg.* 2018. In press.
7. **POSAW Study Group.** Prospective Observational Study on Acute Appendicitis Worldwide (POSAW). *World J Emerg Surg.* 2018;16;13:19.
8. **GlobalSurg Collaborative.** Surgical site infection after gastro-intestinal surgery in high-income, middle-income and low-income countries: a prospective, international, multicentre cohort study. *Lancet Infect Dis.* 2018;18(5):516–525.
9. Mohseni S, Ivarsson J, Ahl R, Dogan S, **Saar S**, Reinsoo A, Sepp T, Isand KG, Garder E, Kaur I, Ruus H, Talving P. Simultaneous common bile duct clearance and laparoscopic cholecystectomy: experience of a one-stage approach. *Eur J Trauma Emerg Surg.* 2018. In press.
10. **Saar S**, Lomp A, Laos J, Mihnovišt V, Šalkauskas R, Lustenberger T, Väli M, Lepner U, Talving P. Population-based Autopsy Study of Traumatic Fatalities. *World J Surg.* 2017;41(7):1790–1795. (*Featured article, July 2017, International Society of Surgery*).
11. **Saar S**, Sokirjanski M, Junkin LK, Laos J, Laar AL, Merioja I, Lepner U, Kukk L, Rimmelgas A, Asser T, Innos K, Starkopf J, Talving P. Evolution of Severe Trauma in Estonia Comparing Time Segments of Early versus Established Independence of the State. *Eur J Trauma Emerg Surg.* 2017;43(6):791–796.

12. Talving P, Rauk ML, Vipp L, Isand KG, Šamarin A, Pöder K, Rätsep I, **Saar S**. Necrosis of the Tail of Pancreas following Proximal Splenic Artery Embolization. *Journal of Surgical Case Reports*. 2016;5:1–4.
13. **Saar S**, Talving P, Laos J, Põdrämägi T, Sokirjanski M, Lustenberger T, Lepner U. Delay Between Onset of Symptoms and Surgery in Acute Appendicitis Increases Perioperative Morbidity: A Prospective Study. *World J Surg*. 2016;40(6):1308–14. (Featured article, June 2016, *International Society of Surgery*).
14. **Saar S**, Merioja I, Lustenberger T, Lepner U, Asser T, Metsvaht T, Ilmoja ML, Kukk L, Starkopf J, Talving P. Severe Trauma in Estonia: 256 consecutive cases analysed and the impact on outcomes comparing two regions. *Eur J Trauma Emerg Surg*. 2016;42(4):497–502.

Eelretsenseerimata

1. **Saar S**, Lepp J, Laar P, Jaanson T, Lipping E, Talving P. Left-sided paraduodenal hernia: review of the literature and a case report. *Eesti Arst*. In press.
2. **Saar S**, Lepp J, Popov A, Novak V, Lepner U, Asser T, Rätsep I, Väli M, Starkopf J, Talving P. Trauma system and outcomes of severely injured patients in Estonia. *Eesti Arst*. 2018;97(11):623–627.
3. **Saar S**, Laars M, Graumann K, Väli M, Ilmoja ML, Rimmelgas A, Lepner U, Starkopf J, Talving P. Pedestrian injuries caused by traffic accidents in Estonia: analysis of 116 consecutive cases from regional hospitals and autopsy reports from forensic science institutions. *Eesti Arst*. 2017;96(11):655–660.
4. Talving P, Mihnovitš V, Lepner U, **Saar S**. Contemporary Management of Acute Appendicitis. *Eesti Arst*. 2016;95(11):723–727. (Best article of the North Estonia Medical Centre, 2016)
5. Talving P, Ilmoja ML, Taal G, Isand KG, Teppo S, Noor EH, Kruusat R, Rimmelgas A, **Saar S**. Blunt Cardiac Rupture in a Toddler. *Journal of Pediatric Surgery Case Reports*. 2016;11:1–3.
6. Talving P, **Saar S**, Lam L. Management of Penetrating Trauma to the Major Abdominal Vessels. *Curr Trauma Rep*. 2016;2:21–8.
7. Nikkolo C, **Saar S**, Sokirjanski M, Junkin LK, Lepner U. Retrospective Study of Surgical Treatment of Primary Hyperparathyroidism at Tartu University Hospital. *Eesti Arst*. 2014;93(11):622–626.

Suulised ettekanded rahvusvahelistel kongressidel

1. **Saar S**, Mihnovitš V, Lustenberger T, Rauk ML, Noor EH, Lipping E, Lomp A, Isand KG, Lepner U, Talving P. Twenty-four hour versus Extended Antibiotic Administration After Surgery in Complicated Appendicitis: A Randomized Controlled Trial. 77th Annual Meeting of the American Association for the Surgery of Trauma, San Diego, USA, Sept 26–29, 2018.

2. **Saar S**, Laos J, Ilmoja ML, Metsvaht T, Laasma M, Märtsen M, Sokirjanski M, Varik K, Talving P. Population-based Pediatric Trauma in Estonia: Forty-eight Consecutive Cases Analyzed. XIV Conference of The Baltic Association of Paediatric Surgery, Estonia, Tartu, May 7, 2016.
3. **Saar S**, Sokirjanski M, Junkin LK, Laos J, Laar AL, Merioja I, Lepner U, Kukk L, Rimmelgas A, Asser T, Innos K, Starkopf J, Talving P. Evolution of Severe Trauma in Estonia Comparing Time Segments of Early versus Established Independence of the State. 17th European Congress of Trauma & Emergency Surgery, Vienna, Austria. April 26, 2016.
4. Soosaar I, **Saar S**, Lomp A, Laos J, Mihnovits V, Shalkauskas R, Väli M, Lustenberger T, Lepner U, Kukk L, Strakopf J, Talving P. Population-based Investigation of Traumatic Vascular Injuries in Estonia: 353 consecutive cases analysed. 17th European Congress of Trauma & Emergency Surgery, Vienna, Austria. April 24, 2016.
5. **Saar S**, Sokirjanski M, Junkin LK, Laos J, Laar AL, Merioja I, Lepner U, Asser T, Ilmoja ML, Kukk L, Rimmelgas A, Talving P. Severe Trauma in Estonia: 254 consecutive cases analysed. 8th Congress of The Baltic Association of Surgeons, Tallinn, Estonia. September 10–12, 2015.

Posterettekanded rahvusvahelistel kongressidel

1. **Saar S**, Reinsoo A, Talving P, Vanakesa T, Saluvere P, Almre I. Esophageal perforations at a referral medical facility: a 17-years perspective. 19th European Congress of Trauma & Emergency Surgery, Valencia, Spain, May 6–8, 2018.
2. Mohseni S, Ivarsson J, Ahl R, Dogan S, **Saar S**, Reinsoo A, Sepp T, Isand KG, Garder E, Kaur I, Ruus H, Talving P. Simultaneous laparoscopic cholecystectomy and intra-operative ERCP for common bile duct stones: Experience of the one-step approach at two referral hospitals. 76th Annual Meeting of AAST and Clinical Congress of Acute Care Surgery, Baltimore, USA, Sept 13–16, 2017.
3. **Saar S**, Lepner U, Laos J, Sokirjanski M, Lustenberger T, Mihnovits V, Lomp A, Talving P. Performance of Diagnostic Modalities in Acute Appendicitis. 47th World Congress of Surgery, Switzerland, Basel, Aug 13–17, 2017.
4. Mihnovits V, **Saar S**, Lomp A, Rajas M, Reinsoo A, Ilves P, Lepner U, Talving P. Risk of Malignancy in Patients with Appendiceal Mass. 47th World Congress of Surgery, Switzerland, Basel, Aug 13–17, 2017.
5. Lomp A, Mihnovits V, **Saar S**, Ilves P, Reim M, Väli M, Talving P, Lepner U. One Hundred and Five Consecutive Liver Injuries Analysed: an Estonian Experience. 18th European Congress of Trauma & Emergency Surgery, Bucharest, Romania, May 7–9, 2017.
6. Einberg M, **Saar S**, Seljanko A, Lomp A, Ruusalepp A, Vanakesa T, Laisaar T, Taal G, Talving P. A 23-years Perspective of Cardiac Injuries at Estonian Major Trauma Facilities. 18th European Congress of Trauma & Emergency Surgery, Bucharest, Romania, May 7–9, 2017.

7. Merioja I, **Saar S**, Laar AL, Laos J, Lomp A, Kontkar K, Seljuškin D, Soosaar I, Tõru T, Avi A, Asser A, Kukk L, Asser T, Starkopf J, Talving P. Population-based investigation on isolated severe traumatic brain injury severity and outcomes in Estonia. EANS 2016, Greece, Athens, September 4–8, 2016.
8. **Saar S**, Merioja I, Lustenberger T, Lepner U, Asser T, Metsvaht T, Ilmoja ML, Kukk L, Talving P. Severe Trauma in Estonia: 256 consecutive cases analysed and the impact on outcomes comparing two regions. 16th European Congress of Trauma & Emergency Surgery, Amsterdam, Netherlands. May 10–12, 2015.

Loengud rahvusvahelistel kongressidel

1. *Severe traumatic brain injury: Estonian perspective*. 14th congress of Baltic Neurosurgical Association, Tartu, Estonia, May 25, 2018.
2. *Trauma system in Estonia: before and after ATLS*. 19th European Congress of Trauma & Emergency Surgery, Valencia, Spain, May 8, 2018.

Loengud kohalikel kongressidel

1. *Non-operative Management of Penetrating Abdominal Trauma*. Clinic 2018. Tartu, Estonia. February 6, 2018.
2. *Severe Trauma in Estonia: 90s vs. nowadays*. Clinic 2017. Tartu, Estonia. January 31, 2017.
3. *Severe Trauma: Estonia vs. South Africa*. Autumn Congress of The North Estonia Medical Centre. Tallinn, Estonia. Oct 30, 2015.
4. *Do helmets save lives?* Researcher's Night. Viimsi, Estonia. Sept 24, 2014.

DISSERTATIONES MEDICINAE UNIVERSITATIS TARTUENSIS

1. **Heidi-Ingrid Maaros.** The natural course of gastric ulcer in connection with chronic gastritis and *Helicobacter pylori*. Tartu, 1991.
2. **Mihkel Zilmer.** Na-pump in normal and tumorous brain tissues: Structural, functional and tumorigenesis aspects. Tartu, 1991.
3. **Eero Vasar.** Role of cholecystokinin receptors in the regulation of behaviour and in the action of haloperidol and diazepam. Tartu, 1992.
4. **Tiina Talvik.** Hypoxic-ischaemic brain damage in neonates (clinical, biochemical and brain computed tomographical investigation). Tartu, 1992.
5. **Ants Peetsalu.** Vagotomy in duodenal ulcer disease: A study of gastric acidity, serum pepsinogen I, gastric mucosal histology and *Helicobacter pylori*. Tartu, 1992.
6. **Marika Mikelsaar.** Evaluation of the gastrointestinal microbial ecosystem in health and disease. Tartu, 1992.
7. **Hele Everaus.** Immuno-hormonal interactions in chronic lymphocytic leukaemia and multiple myeloma. Tartu, 1993.
8. **Ruth Mikelsaar.** Etiological factors of diseases in genetically consulted children and newborn screening: dissertation for the commencement of the degree of doctor of medical sciences. Tartu, 1993.
9. **Agu Tamm.** On metabolic action of intestinal microflora: clinical aspects. Tartu, 1993.
10. **Katrin Gross.** Multiple sclerosis in South-Estonia (epidemiological and computed tomographical investigations). Tartu, 1993.
11. **Oivi Uibo.** Childhood coeliac disease in Estonia: occurrence, screening, diagnosis and clinical characterization. Tartu, 1994.
12. **Viiu Tuulik.** The functional disorders of central nervous system of chemistry workers. Tartu, 1994.
13. **Margus Viigimaa.** Primary haemostasis, antiaggregative and anticoagulant treatment of acute myocardial infarction. Tartu, 1994.
14. **Rein Kolk.** Atrial versus ventricular pacing in patients with sick sinus syndrome. Tartu, 1994.
15. **Toomas Podar.** Incidence of childhood onset type 1 diabetes mellitus in Estonia. Tartu, 1994.
16. **Kiira Subi.** The laboratory surveillance of the acute respiratory viral infections in Estonia. Tartu, 1995.
17. **Irja Lutsar.** Infections of the central nervous system in children (epidemiologic, diagnostic and therapeutic aspects, long term outcome). Tartu, 1995.
18. **Aavo Lang.** The role of dopamine, 5-hydroxytryptamine, sigma and NMDA receptors in the action of antipsychotic drugs. Tartu, 1995.
19. **Andrus Arak.** Factors influencing the survival of patients after radical surgery for gastric cancer. Tartu, 1996.

20. **Tõnis Karki.** Quantitative composition of the human lactoflora and method for its examination. Tartu, 1996.
21. **Reet Mändar.** Vaginal microflora during pregnancy and its transmission to newborn. Tartu, 1996.
22. **Triin Remmel.** Primary biliary cirrhosis in Estonia: epidemiology, clinical characterization and prognostication of the course of the disease. Tartu, 1996.
23. **Toomas Kivastik.** Mechanisms of drug addiction: focus on positive reinforcing properties of morphine. Tartu, 1996.
24. **Paavo Pokk.** Stress due to sleep deprivation: focus on GABA_A receptor-chloride ionophore complex. Tartu, 1996.
25. **Kristina Allikmets.** Renin system activity in essential hypertension. Associations with atherothrombotic cardiovascular risk factors and with the efficacy of calcium antagonist treatment. Tartu, 1996.
26. **Triin Parik.** Oxidative stress in essential hypertension: Associations with metabolic disturbances and the effects of calcium antagonist treatment. Tartu, 1996.
27. **Svetlana Päi.** Factors promoting heterogeneity of the course of rheumatoid arthritis. Tartu, 1997.
28. **Maarike Sallo.** Studies on habitual physical activity and aerobic fitness in 4 to 10 years old children. Tartu, 1997.
29. **Paul Naaber.** *Clostridium difficile* infection and intestinal microbial ecology. Tartu, 1997.
30. **Rein Pähkla.** Studies in pinoline pharmacology. Tartu, 1997.
31. **Andrus Juhan Voitk.** Outpatient laparoscopic cholecystectomy. Tartu, 1997.
32. **Joel Starkopf.** Oxidative stress and ischaemia-reperfusion of the heart. Tartu, 1997.
33. **Janika Kõrv.** Incidence, case-fatality and outcome of stroke. Tartu, 1998.
34. **Ülla Linnamägi.** Changes in local cerebral blood flow and lipid peroxidation following lead exposure in experiment. Tartu, 1998.
35. **Ave Minajeva.** Sarcoplasmic reticulum function: comparison of atrial and ventricular myocardium. Tartu, 1998.
36. **Oleg Milenin.** Reconstruction of cervical part of esophagus by revascularised ileal autografts in dogs. A new complex multistage method. Tartu, 1998.
37. **Sergei Pakriev.** Prevalence of depression, harmful use of alcohol and alcohol dependence among rural population in Udmurtia. Tartu, 1998.
38. **Allen Kaasik.** Thyroid hormone control over β -adrenergic signalling system in rat atria. Tartu, 1998.
39. **Vallo Matto.** Pharmacological studies on anxiogenic and antiaggressive properties of antidepressants. Tartu, 1998.
40. **Maire Vasar.** Allergic diseases and bronchial hyperreactivity in Estonian children in relation to environmental influences. Tartu, 1998.
41. **Kaja Julge.** Humoral immune responses to allergens in early childhood. Tartu, 1998.

42. **Heli Grünberg.** The cardiovascular risk of Estonian schoolchildren. A cross-sectional study of 9-, 12- and 15-year-old children. Tartu, 1998.
43. **Epp Sepp.** Formation of intestinal microbial ecosystem in children. Tartu, 1998.
44. **Mai Ots.** Characteristics of the progression of human and experimental glomerulopathies. Tartu, 1998.
45. **Tiina Ristimäe.** Heart rate variability in patients with coronary artery disease. Tartu, 1998.
46. **Leho Kõiv.** Reaction of the sympatho-adrenal and hypothalamo-pituitary-adrenocortical system in the acute stage of head injury. Tartu, 1998.
47. **Bela Adojaan.** Immune and genetic factors of childhood onset IDDM in Estonia. An epidemiological study. Tartu, 1999.
48. **Jakov Shlik.** Psychophysiological effects of cholecystokinin in humans. Tartu, 1999.
49. **Kai Kisand.** Autoantibodies against dehydrogenases of α -ketoacids. Tartu, 1999.
50. **Toomas Marandi.** Drug treatment of depression in Estonia. Tartu, 1999.
51. **Ants Kask.** Behavioural studies on neuropeptide Y. Tartu, 1999.
52. **Ello-Rahel Karelson.** Modulation of adenylate cyclase activity in the rat hippocampus by neuropeptide galanin and its chimeric analogs. Tartu, 1999.
53. **Tanel Laisaar.** Treatment of pleural empyema — special reference to intrapleural therapy with streptokinase and surgical treatment modalities. Tartu, 1999.
54. **Eve Pihl.** Cardiovascular risk factors in middle-aged former athletes. Tartu, 1999.
55. **Katrin Õunap.** Phenylketonuria in Estonia: incidence, newborn screening, diagnosis, clinical characterization and genotype/phenotype correlation. Tartu, 1999.
56. **Siiri Kõljalg.** *Acinetobacter* – an important nosocomial pathogen. Tartu, 1999.
57. **Helle Karro.** Reproductive health and pregnancy outcome in Estonia: association with different factors. Tartu, 1999.
58. **Heili Varendi.** Behavioral effects observed in human newborns during exposure to naturally occurring odors. Tartu, 1999.
59. **Anneli Beilmann.** Epidemiology of epilepsy in children and adolescents in Estonia. Prevalence, incidence, and clinical characteristics. Tartu, 1999.
60. **Vallo Volke.** Pharmacological and biochemical studies on nitric oxide in the regulation of behaviour. Tartu, 1999.
61. **Pilvi Ilves.** Hypoxic-ischaemic encephalopathy in asphyxiated term infants. A prospective clinical, biochemical, ultrasonographical study. Tartu, 1999.
62. **Anti Kalda.** Oxygen-glucose deprivation-induced neuronal death and its pharmacological prevention in cerebellar granule cells. Tartu, 1999.
63. **Eve-Irene Lepist.** Oral peptide prodrugs – studies on stability and absorption. Tartu, 2000.

64. **Jana Kivastik.** Lung function in Estonian schoolchildren: relationship with anthropometric indices and respiratory symptoms, reference values for dynamic spirometry. Tartu, 2000.
65. **Karin Kull.** Inflammatory bowel disease: an immunogenetic study. Tartu, 2000.
66. **Kaire Innos.** Epidemiological resources in Estonia: data sources, their quality and feasibility of cohort studies. Tartu, 2000.
67. **Tamara Vorobjova.** Immune response to *Helicobacter pylori* and its association with dynamics of chronic gastritis and epithelial cell turnover in antrum and corpus. Tartu, 2001.
68. **Ruth Kalda.** Structure and outcome of family practice quality in the changing health care system of Estonia. Tartu, 2001.
69. **Annika Krüüner.** *Mycobacterium tuberculosis* – spread and drug resistance in Estonia. Tartu, 2001.
70. **Marlit Veldi.** Obstructive Sleep Apnoea: Computerized Endopharyngeal Myotonometry of the Soft Palate and Lingual Musculature. Tartu, 2001.
71. **Anneli Uusküla.** Epidemiology of sexually transmitted diseases in Estonia in 1990–2000. Tartu, 2001.
72. **Ade Kallas.** Characterization of antibodies to coagulation factor VIII. Tartu, 2002.
73. **Heidi Annuk.** Selection of medicinal plants and intestinal lactobacilli as antimicrobial components for functional foods. Tartu, 2002.
74. **Aet Lukmann.** Early rehabilitation of patients with ischaemic heart disease after surgical revascularization of the myocardium: assessment of health-related quality of life, cardiopulmonary reserve and oxidative stress. A clinical study. Tartu, 2002.
75. **Maigi Eisen.** Pathogenesis of Contact Dermatitis: participation of Oxidative Stress. A clinical – biochemical study. Tartu, 2002.
76. **Piret Hussar.** Histology of the post-traumatic bone repair in rats. Elaboration and use of a new standardized experimental model – bicortical perforation of tibia compared to internal fracture and resection osteotomy. Tartu, 2002.
77. **Tõnu Rätsep.** Aneurysmal subarachnoid haemorrhage: Noninvasive monitoring of cerebral haemodynamics. Tartu, 2002.
78. **Marju Herodes.** Quality of life of people with epilepsy in Estonia. Tartu, 2003.
79. **Katre Maasalu.** Changes in bone quality due to age and genetic disorders and their clinical expressions in Estonia. Tartu, 2003.
80. **Toomas Sillakivi.** Perforated peptic ulcer in Estonia: epidemiology, risk factors and relations with *Helicobacter pylori*. Tartu, 2003.
81. **Leena Puksa.** Late responses in motor nerve conduction studies. F and A waves in normal subjects and patients with neuropathies. Tartu, 2003.
82. **Krista Lõivukene.** *Helicobacter pylori* in gastric microbial ecology and its antimicrobial susceptibility pattern. Tartu, 2003.

83. **Helgi Kolk.** Dyspepsia and *Helicobacter pylori* infection: the diagnostic value of symptoms, treatment and follow-up of patients referred for upper gastrointestinal endoscopy by family physicians. Tartu, 2003.
84. **Helena Soomer.** Validation of identification and age estimation methods in forensic odontology. Tartu, 2003.
85. **Kersti Oselin.** Studies on the human MDR1, MRP1, and MRP2 ABC transporters: functional relevance of the genetic polymorphisms in the *MDR1* and *MRP1* gene. Tartu, 2003.
86. **Jaan Soplepmann.** Peptic ulcer haemorrhage in Estonia: epidemiology, prognostic factors, treatment and outcome. Tartu, 2003.
87. **Margot Peetsalu.** Long-term follow-up after vagotomy in duodenal ulcer disease: recurrent ulcer, changes in the function, morphology and *Helicobacter pylori* colonisation of the gastric mucosa. Tartu, 2003.
88. **Kersti Klaamas.** Humoral immune response to *Helicobacter pylori* a study of host-dependent and microbial factors. Tartu, 2003.
89. **Pille Taba.** Epidemiology of Parkinson's disease in Tartu, Estonia. Prevalence, incidence, clinical characteristics, and pharmacoepidemiology. Tartu, 2003.
90. **Alar Veraksitš.** Characterization of behavioural and biochemical phenotype of cholecystokinin-2 receptor deficient mice: changes in the function of the dopamine and endopioidergic system. Tartu, 2003.
91. **Ingrid Kalev.** CC-chemokine receptor 5 (CCR5) gene polymorphism in Estonians and in patients with Type I and Type II diabetes mellitus. Tartu, 2003.
92. **Lumme Kadaja.** Molecular approach to the regulation of mitochondrial function in oxidative muscle cells. Tartu, 2003.
93. **Aive Liigant.** Epidemiology of primary central nervous system tumours in Estonia from 1986 to 1996. Clinical characteristics, incidence, survival and prognostic factors. Tartu, 2004.
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95. **Mari Järvelaid.** Health damaging risk behaviours in adolescence. Tartu, 2004.
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97. **Gunnar Tasa.** Polymorphic glutathione S-transferases – biology and role in modifying genetic susceptibility to senile cataract and primary open angle glaucoma. Tartu, 2004.
98. **Tuuli Käämbre.** Intracellular energetic unit: structural and functional aspects. Tartu, 2004.
99. **Vitali Vassiljev.** Influence of nitric oxide synthase inhibitors on the effects of ethanol after acute and chronic ethanol administration and withdrawal. Tartu, 2004.

100. **Aune Rehema.** Assessment of nonhaem ferrous iron and glutathione redox ratio as markers of pathogeneticity of oxidative stress in different clinical groups. Tartu, 2004.
101. **Evelin Seppet.** Interaction of mitochondria and ATPases in oxidative muscle cells in normal and pathological conditions. Tartu, 2004.
102. **Eduard Maron.** Serotonin function in panic disorder: from clinical experiments to brain imaging and genetics. Tartu, 2004.
103. **Marje Oona.** *Helicobacter pylori* infection in children: epidemiological and therapeutic aspects. Tartu, 2004.
104. **Kersti Kokk.** Regulation of active and passive molecular transport in the testis. Tartu, 2005.
105. **Vladimir Järv.** Cross-sectional imaging for pretreatment evaluation and follow-up of pelvic malignant tumours. Tartu, 2005.
106. **Andre Õun.** Epidemiology of adult epilepsy in Tartu, Estonia. Incidence, prevalence and medical treatment. Tartu, 2005.
107. **Piibe Muda.** Homocysteine and hypertension: associations between homocysteine and essential hypertension in treated and untreated hypertensive patients with and without coronary artery disease. Tartu, 2005.
108. **Küllü Kingo.** The interleukin-10 family cytokines gene polymorphisms in plaque psoriasis. Tartu, 2005.
109. **Mati Merila.** Anatomy and clinical relevance of the glenohumeral joint capsule and ligaments. Tartu, 2005.
110. **Epp Songisepp.** Evaluation of technological and functional properties of the new probiotic *Lactobacillus fermentum* ME-3. Tartu, 2005.
111. **Tiia Ainla.** Acute myocardial infarction in Estonia: clinical characteristics, management and outcome. Tartu, 2005.
112. **Andres Sell.** Determining the minimum local anaesthetic requirements for hip replacement surgery under spinal anaesthesia – a study employing a spinal catheter. Tartu, 2005.
113. **Tiia Tamme.** Epidemiology of odontogenic tumours in Estonia. Pathogenesis and clinical behaviour of ameloblastoma. Tartu, 2005.
114. **Triine Annus.** Allergy in Estonian schoolchildren: time trends and characteristics. Tartu, 2005.
115. **Tiia Voor.** Microorganisms in infancy and development of allergy: comparison of Estonian and Swedish children. Tartu, 2005.
116. **Priit Kasenõmm.** Indicators for tonsillectomy in adults with recurrent tonsillitis – clinical, microbiological and pathomorphological investigations. Tartu, 2005.
117. **Eva Zusinaite.** Hepatitis C virus: genotype identification and interactions between viral proteases. Tartu, 2005.
118. **Piret Kõll.** Oral lactoflora in chronic periodontitis and periodontal health. Tartu, 2006.
119. **Tiina Stelmach.** Epidemiology of cerebral palsy and unfavourable neurodevelopmental outcome in child population of Tartu city and county, Estonia Prevalence, clinical features and risk factors. Tartu, 2006.

120. **Katrin Pudersell.** Tropane alkaloid production and riboflavine excretion in the field and tissue cultures of henbane (*Hyoscyamus niger* L.). Tartu, 2006.
121. **Külli Jaako.** Studies on the role of neurogenesis in brain plasticity. Tartu, 2006.
122. **Aare Märtsen.** Lower limb lengthening: experimental studies of bone regeneration and long-term clinical results. Tartu, 2006.
123. **Heli Tähepõld.** Patient consultation in family medicine. Tartu, 2006.
124. **Stanislav Liskmann.** Peri-implant disease: pathogenesis, diagnosis and treatment in view of both inflammation and oxidative stress profiling. Tartu, 2006.
125. **Ruth Rudissaar.** Neuropharmacology of atypical antipsychotics and an animal model of psychosis. Tartu, 2006.
126. **Helena Andreson.** Diversity of *Helicobacter pylori* genotypes in Estonian patients with chronic inflammatory gastric diseases. Tartu, 2006.
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