Time to Surgery Is Associated with Thirty-Day and Ninety-Day Mortality After Proximal Femoral Fracture

A Retrospective Observational Study on Prospectively Collected Data from the Danish Fracture Database Collaborators

Anne Marie Nyholm, MD, Kirill Gromov, MD, PhD, Henrik Palm, MD, Michael Brix, MD, Thomas Kallemose, MSc, Anders Troelsen, MD, and the Danish Fracture Database Collaborators*

Investigation performed at Clinical Orthopaedic Research Hvidovre (CORH), Department of Orthopaedic Surgery, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark

Background: We hypothesized that undergoing surgery as soon as possible reduces early mortality in patients with a proximal femoral fracture. Our aim was to evaluate the association between surgical delay and early mortality in these patients.

Methods: We performed a retrospective analysis of prospectively collected data from the Danish Fracture Database and the Civil Registration System on patients who were fifty years of age or older and had undergone surgery for a proximal femoral fracture. Femoral head fracture (classified as OTA/AO 31C per the OTA/AO classification system), high-energy trauma, pathological fractures, multiple fractures, and surgeries performed with implants not commonly used were excluded. End points were adjusted odds ratios for thirty-day and ninety-day mortality.

Results: For the 3517 surgeries included in this study, the median patient age was 82.0 years (range, fifty-one to 107 years), 2458 patients (70%) were female, and 1720 surgeries (49%) were performed because of a trochanteric fracture. Within twelve hours, 722 of the surgeries (21%) had been performed; within twenty-four hours, 2482 surgeries (71%); within thirty-six hours, 3024 surgeries (86%); within forty-eight hours, 3242 surgeries (92%); and within seventy-two hours, 3353 surgeries (95%). Unsupervised surgeons with an education level below that of an attending surgeon performed the surgery in 1807 (51%) of all cases. The thirty-day mortality was 380 (10.8%) and the ninety-day mortality was 612 (17.4%). The risk of thirty-day mortality increased with a surgical delay of more than twelve hours (odds ratio, 1.45; $p = 0.02$), more than twenty-four hours (odds ratio, 1.34; $p = 0.02$), and more than forty-eight hours (odds ratio, 1.56; $p = 0.02$); the risk of ninety-day mortality increased with a surgical delay of more than twenty-four hours (odds ratio, 1.23; $p = 0.04$). An education level of the surgeon below that of an attending surgeon increased the risk of thirty-day mortality (odds ratio, 1.28; $p = 0.035$) and ninety-day mortality (odds ratio, 1.26; $p = 0.016$). Increasing American Society of Anesthesiologists score and male sex significantly increased both thirty-day and ninety-day mortality.

continued

Peer Review: This article was reviewed by the Editor-in-Chief and one Deputy Editor, and it underwent blinded review by two or more outside experts. The Deputy Editor reviewed each revision of the article, and it underwent a final review by the Editor-in-Chief prior to publication. Final corrections and clarifications occurred during one or more exchanges between the author(s) and copyeditors.

*The Danish Fracture Database Collaborators: Anders Wallin Paulsen, John K. Petersen, Thomas Bloch, Kim Stentzer, Anders Jordy, Lasse Birkelund, Lars Tambour Hansen, Peder Klement, Jes Røndbjerg, Stephan Kantak, and Steffen Skov Jensen.

Disclosure: None of the authors received payments or services, either directly or indirectly (i.e., via his or her institution), from a third party in support of any aspect of this work. One or more of the authors, or his or her institution, has had a financial relationship, in the thirty-six months prior to submission of this work, with an entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work. Also, one or more of the authors has had another relationship, or has engaged in another activity, that could be perceived to influence or have the potential to influence what is written in this work. The complete **Disclosures of Potential Conflicts of Interest** submitted by authors are always provided with the online version of the article.

Conclusions: In this study, a surgical delay of more than twelve hours significantly increased the adjusted risk of thirty-day mortality and a surgical delay of more than twenty-four hours significantly increased the adjusted risk of ninety-day mortality. The adjusted risk of both thirty-day and ninety-day mortality increased significantly when the education level of the surgeon was below that of an attending surgeon. The study findings challenge orthopaedic departments to facilitate fast surgical treatment supported by attending orthopaedic surgeons.

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Short-term mortality is used as a quality indicator for the treatment of proximal femoral fractures. In Denmark, with a defined goal of thirty-day mortality below 10%[1], a number of patient-related, non-modifiable factors, such as age, sex, American Society of Anesthesiologists (ASA) score, functional impairment, and type of fracture, have been identified as increasing early mortality[2]. Other, modifiable factors, not directly related to the patient, have also been identified, such as the method of fracture treatment[3].

Surgical delay has been suggested as a modifiable risk factor for early mortality. Although surgical delay has been associated with an increased length of stay and a higher risk of postoperative complications[4-7], the exact association with mortality is less clear. Some studies have shown that a surgical delay of more than twenty-four hours or more than forty-eight hours significantly increases mortality[8-15], although other studies found no association[4,6,16-18]. A meta-analysis has found that a surgical delay of more than forty-eight hours increases mortality[9]. To date, no adverse effects of a short surgical delay (less than forty-eight hours) have been identified[7].

The aim of this study was to investigate whether a surgical delay of more than twelve hours, more than twenty-four hours, more than thirty-six hours, more than forty-eight hours, and more than seventy-two hours increases thirty-day and ninety-day mortality rates for patients with proximal femoral fractures and to identify other potentially modifiable factors that increase this mortality. Our hypothesis was that surgery as soon as possible after diagnosis is associated with the lowest mortality.

Materials and Methods

The protocol with defined hypothesis and outcome measures was written and the study was approved by the Danish Data Protection Agency prior to data collection and analysis (see Appendix).

Patient and surgery-related data were collected from the Danish Fracture Database, which was established in 2011 as an online-based database for the registration of fracture-related surgery[19]. The data are entered in the database by the surgeon immediately after the surgical procedures and include patient-related, trauma-related, and surgery-related factors[20]. All fractures are classified according to the OTA/AO classification[21]. Nineteen hospitals across Denmark, covering approximately 90% of the population, are currently participating in the Danish Fracture Database collaboration, with approximately 30,000 registered procedures.

From the Danish Fracture Database, we identified consecutive primary surgical procedures performed up until May 14, 2014, for a primary proximal femoral fracture (classified as OTA/AO 31) in patients who were at least fifty years of age. Only data from centers with a total of fifty or more registered procedures were included in this study (thirteen centers, 3985 procedures). To minimize potential confounding factors and make the study group as homogenous as possible, we excluded from the study patients undergoing surgical procedures for articular fracture of the femoral head (classified as OTA/AO 31C) (n = 12), pathological fracture (n = 41), or high-energy trauma in which a specialized trauma team was assembled upon arrival (n = 51); patients who were younger than fifty years (n = 195); patients who underwent surgery in which the type of osteosynthesis was different from commonly used fixation methods (i.e., external fixation, locking compression plates) (n = 78); and patients with missing data (n = 90). One patient had both a pathological fracture and a high-energy trauma and was also excluded (n = 1). This left 3517 surgical procedures for analysis.

Data included age, sex, type of fracture, type of surgery, ASA score, surgical delay, and education level of the surgeon. Surgical delay was defined as the time in hours from the radiographic diagnosis of the fracture until the start of the surgical procedure and was divided into groups: twelve hours or less, more than twelve hours to twenty-four hours, more than twenty-four hours to thirty-six hours, more than thirty-six hours to forty-eight hours, more than forty-eight hours to seventy-two hours, and more than seventy-two hours. The type of surgery was categorized as arthroplasty, sliding hip screw, intramedullary nail, or cannulated screws (including hook pins). The education level of the surgeon was classified as attending or above if an attending or higher-level surgeon either performed or supervised the procedure (the attending or higher-level surgeon was present within the operating theater). All other surgeons were classified as having an education level below that of an attending surgeon. End points were defined as thirty-day mortality and ninety-day mortality. Mortality data were collected from the Civil Registration System, which has information on the vital status of all Danish citizens including changes in address, date of emigration, and date of death[22].

A multivariate logistic regression analysis was performed on the basis of each surgical delay group to calculate the adjusted thirty-day and ninety-day mortality rates for the particular group. All analyses were adjusted for other recorded variables of age (ten-year intervals), sex (male or female), ASA score (1, 2, 3, or 4), fracture type (femoral neck or trochanteric), type of surgery, and education level of the surgeon. Furthermore, all other variables were tested

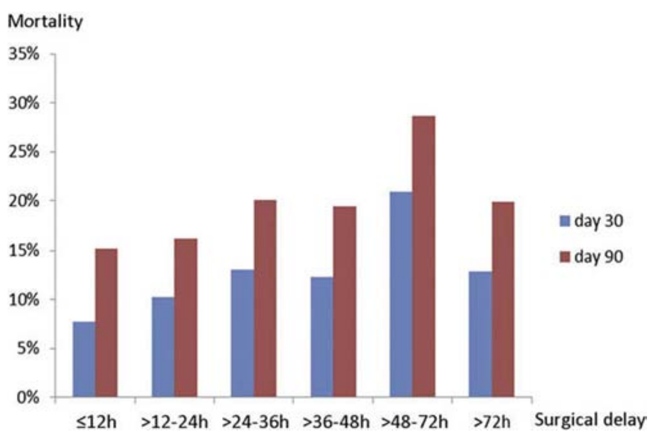

Fig. 1
A bar graph showing mortality stratified according to surgical delay.

TABLE I Patient Demographic Characteristics Stratified According to Surgical Delay*

	Surgical Delay						
	≤12 Hr	>12 to 24 Hr	>24 to 36 Hr	>36 to 48 Hr	>48 to 72 Hr	>72 Hr	Total
No. of patients†	722 (20.5)	1760 (50.0)	542 (15.4)	218 (6.2)	111 (3.2)	164 (4.7)	3517
Age in yr							
50 to 59	51 (7.1)	99 (5.6)	27 (5.0)	10 (4.6)	5 (4.5)	10 (6.1)	202 (5.7)
60 to 69	118 (16.3)	224 (12.7)	71 (13.1)	22 (10.1)	18 (16.2)	21 (12.8)	474 (13.5)
70 to 79	166 (23.0)	454 (25.8)	130 (24.0)	55 (25.2)	32 (28.8)	44 (26.8)	881 (25.0)
80 to 89	285 (39.5)	728 (41.4)	222 (41.0)	91 (41.7)	35 (31.5)	60 (36.6)	1421 (40.4)
90 to 99	99 (13.7)	250 (14.2)	89 (16.4)	39 (17.9)	21 (18.9)	28 (17.1)	526 (15.0)
≥100	3 (0.4)	5 (0.3)	3 (0.6)	1 (0.5)	0 (0)	1 (0.6)	13 (0.4)
Sex							
Female	512 (70.9)	1236 (70.2)	365 (67.3)	147 (67.4)	77 (69.4)	121 (73.8)	2458 (69.9)
Male	210 (29.1)	524 (29.8)	177 (32.7)	71 (32.6)	34 (30.6)	43 (26.2)	1059 (30.1)
ASA score							
1	49 (6.8)	120 (6.8)	50 (9.2)	12 (5.5)	8 (7.2)	14 (8.5)	253 (7.2)
2	381 (52.8)	873 (49.6)	233 (43.0)	93 (42.7)	36 (32.4)	69 (42.1)	1685 (47.9)
3	266 (36.8)	700 (39.8)	243 (44.8)	101 (46.3)	54 (48.6)	66 (40.2)	1430 (40.7)
4	26 (3.6)	60 (3.4)	23 (4.2)	12 (5.5)	13 (11.7)	15 (9.1)	149 (4.2)
5	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Type of fracture							
Trochanteric	388 (53.7)	844 (48.0)	274 (50.6)	103 (47.2)	39 (35.1)	72 (43.9)	1720 (48.9)
Femoral neck	334 (46.3)	916 (52.0)	268 (49.4)	115 (52.8)	72 (64.9)	92 (56.1)	1797 (51.1)
Education level of surgeon							
Attending or above	356 (49.3)	798 (45.3)	283 (52.2)	113 (51.8)	64 (57.7)	96 (58.5)	1710 (48.6)
Below attending	366 (50.7)	962 (54.7)	259 (47.8)	105 (48.2)	47 (42.3)	68 (41.5)	1807 (51.4)
Type of surgery							
Intramedullary nail	269 (37.3)	628 (35.7)	199 (36.7)	75 (34.4)	26 (23.4)	51 (31.1)	1248 (35.5)
Dynamic hip screw	142 (19.7)	279 (15.9)	101 (18.6)	35 (16.1)	20 (18.0)	27 (16.5)	604 (17.2)
Arthroplasty	171 (23.7)	603 (34.3)	180 (33.2)	84 (38.5)	50 (45.0)	65 (39.6)	1153 (32.8)
Cannulated screw	140 (19.4)	250 (14.2)	62 (11.4)	24 (11.0)	15 (13.5)	21 (12.8)	512 (14.6)
Mortality							
Thirty days	56 (7.8)	182 (10.3)	70 (12.9)	27 (12.4)	23 (20.7)	22 (13.4)	380 (10.8)
Ninety days	110 (15.2)	287 (16.3)	108 (19.9)	43 (19.7)	32 (28.8)	32 (19.5)	612 (17.4)

*The values are given as the number of patients, with the percentage in parentheses. †The percentage values are based on the total number of patients. All other percentage values are within the allocated delay group.

similarly with adjustment for surgical delay. A simultaneous test (a test for overall effect), using the type-III test with the chi-square test statistics, was used to test the effect of the variables in the model. A model with continuous delay time was constructed, but showed a similar change in probability over delay time as in the disjoint model. Therefore, because the disjoint model was directly related to the aim and the continuous model did not provide much new information, we chose to use the disjoint model. All analysis was performed with use of R (version 3.0.2; R Foundation for Statistical Computing, Vienna, Austria). Significance was set at $p < 0.05$.

Source of Funding

The study was funded by the Department of Orthopaedic Surgery, Hvidovre University Hospital, Copenhagen, Denmark, which is the employer of five authors in this study (A.M.N., A.T., H.P., K.G, and T.K.).

Results

The median patient age was 82.0 years (range, fifty-one to 107 years) and 2458 patients (69.9%) were female. With regard to ASA scores, 253 patients (7.2%) had a score of 1, 1685 (47.9%) had a score of 2, 1430 (40.7%) had a score of 3, and 149 (4.2%) had a score of 4. The surgeries were classified according to the OTA/AO system, and 1720 surgeries (49%) were for a trochanteric fracture (OTA/AO 31A) and 1797 (51%) were for a femoral neck fracture (OTA/AO 31B). Within twelve hours, 722 patients (21%) had undergone surgery; within twenty-four hours, 2482 (71%) had; within thirty-six hours, 3024 (86%) had; within forty-eight hours, 3242 (92%) had; and within seventy-two

TABLE II Risk of Mortality Calculated with Use of Logistic Regression

	Thirty-Day Mortality Risk		Ninety-Day Mortality Risk	
	OR*	P Value	OR*	P Value
Surgical delay in hr				
>12 compared with ≤12	1.45 (1.06 to 1.99)	0.0206	1.10 (0.86 to 1.40)	0.4410
>24 compared with ≤24	1.34 (1.06 to 1.70)	0.0152	1.23 (1.00 to 1.50)	0.0449
>36 compared with ≤36	1.32 (0.98 to 1.78)	0.0696	1.21 (0.94 to 1.56)	0.1356
>48 compared with ≤48	1.56 (1.07 to 2.26)	0.0192	1.36 (0.98 to 1.89)	0.0617
>72 compared with ≤72	1.23 (0.74 to 2.02)	0.5733	1.09 (0.71 to 1.68)	0.6891
Type of surgery		0.0229†		0.2972†
Intramedullary nail	1		1	
Dynamic hip screw	0.73 (0.51 to 1.05)	0.0899	0.83 (0.62 to 1.12)	0.2165
Arthroplasty	0.96 (0.48 to 1.93)	0.9153	0.78 (0.45 to 1.36)	0.3891
Cannulated screw	0.56 (0.26 to 1.20)	0.1363	0.63 (0.35 to 1.14)	0.1255
ASA score		<0.001†		<0.001†
1	1		1	
2	3.00 (1.08 to 8.32)	0.0349	2.96 (1.36 to 6.46)	0.0064
3	5.94 (2.16 to 16.39)	0.0006	6.93 (3.19 to 15.04)	<0.001
4	29.87 (10.36 to 86.13)	<0.001	27.78 (12.04 to 64.07)	<0.001
Sex				
Female	1		1	
Male	2.08 (1.64 to 2.65)	<0.001	1.93 (1.57 to 2.36)	<0.001
Education level of surgeon				
Attending or above	1		1	
Below attending	1.28 (1.02 to 1.61)	0.0350	1.26 (1.05 to 1.53)	0.0158
Type of fracture				
Femoral neck	1		1	
Trochanteric	1.06 (0.55 to 2.04)	0.8574	1.28 (0.77 to 2.13)	0.3421
Age in yr		<0.001†		<0.001†
50 to 59	1		1	
60 to 69	3.28 (0.95 to 11.29)	0.0596	2.53 (1.09 to 5.86)	0.0306
70 to 79	3.93 (1.19 to 13.01)	0.0251	3.02 (1.35 to 6.78)	0.0073
80 to 89	9.35 (2.89 to 30.26)	0.0002	7.25 (3.30 to 15.95)	<0.001
90 to 99	17.02 (5.19 to 55.84)	<0.001	13.13 (5.87 to 29.34)	<0.001
≥100	76.42 (14.76 to 395.63)	<0.001	39.70 (9.91 to 159.06)	<0.001

*The values are given as the odds ratio, with the 95% confidence interval in parentheses. †These p values were determined with use of the test for overall effect.

hours, 3353 (95%) had. A surgeon with an education of an attending surgeon or above performed or supervised the surgery in 1710 (49%) of all cases (Table I).

Mortality was 10.8% at thirty days and 17.4% at ninety days (Table I). The incidence of death increased with increasing surgical delay at both thirty days and ninety days (Table I, Fig. 1).

An increased risk of thirty-day mortality was estimated for all surgical delay groups, but only surgical delay of more than twelve hours compared with twelve hours or less (adjusted odds ratio [OR], 1.45; p = 0.021), surgical delay of more than twenty-four hours compared with twenty-four hours or less (OR, 1.34; p = 0.015), and surgical delay of more than forty-eight hours compared with forty-eight hours or less (OR, 1.56; p = 0.019) showed a significantly higher risk of thirty-day mortality. Likewise, all estimates for ninety-day mortality showed an increased risk; however, the effect was only significant for surgical delay of more than twenty-four hours compared with twenty-four hours or less (OR, 1.23; p = 0.045) (Table II).

The effect of the other factors included in the models (age, sex, ASA score, fracture type, treatment, and education level of surgeon) on mortality varied across the models for the different surgical delay groups for thirty and ninety-day mortality; however, the effects did not change enough to change the interpretation of the ORs or whether they were significant ($p < 0.05$). Therefore, only estimates from the model with the surgical delay groups of twelve hours or less and more than twelve hours are reported in Table II. Type-III tests showed that ASA score, sex, education level of surgeon, and patient age had a significant effect ($p < 0.05$) in the models for thirty and ninety-day mortality, but treatment only showed a significant effect ($p < 0.05$) in the thirty-day mortality models. Both thirty and ninety-day mortality increased with increased ASA score, male sex, education level of the surgeon below that of an attending surgeon, and increasing patient age (Table II).

Discussion

In this study, we found that a surgical delay of more than twelve hours, more than twenty-four hours, and more than forty-eight hours significantly increased the adjusted risk of thirty-day mortality and that a surgical delay of more than twenty-four hours significantly increased the adjusted risk of ninety-day mortality. Our hypothesis that surgery as soon as possible reduces early mortality was supported with regard to thirty-day mortality, but not for ninety-day mortality. Furthermore, we found a significant increase in the risk of mortality when surgery is performed by an unsupervised surgeon with an education level below that of an attending surgeon.

Our data were derived from a database in which a large number of clinically relevant factors are registered prospectively by the surgeon performing the surgery directly after completing the procedure[20], thus minimizing the risk of data inaccuracy. Even so, this study had limitations attributable to the nature of data collected in a registry. Surgical delay is defined as time from radiographic diagnosis to onset of surgery, which should be taken into account when comparing with previous studies. This definition is used in the Danish Fracture Database because the time of injury is often difficult to identify and we want to evaluate modifiable factors, which we do not consider time from injury to diagnosis to be. The definition also allows fractures sustained in the hospital to be included, which in Denmark account for 7% of all proximal femoral fractures[23]. The registry only includes some of the factors hypothetically influencing short-term mortality after surgery; thus, functional impairment, actual diagnosis of comorbidities, mental health, admission on weekends or holidays, cause of delay, hospital size, early mobilization, a multidisciplinary and multimodal standardized approach, and type of anesthesia are not taken into account, and further conclusions about the relation of specific comorbidities or other factors not included in the database and surgical delay are not possible on the basis of our data. We have statistically been able to adjust for the major confounding factors such as age, sex, and ASA score, as well as type of fracture, type of surgery, and surgical expertise, but still we cannot distinguish between association and causality with regard to the relation between surgical delay and mortality. Determining whether delay in the individual patient increases the mortality risk would require a randomized design of shorter compared with longer delay, which in our view is not ethical and perhaps not feasible; thus, a registry study like ours may represent the highest possible evidence level.

To our knowledge, our study was among the first of this sample size to consider so many clinically relevant factors. Most of our findings were in accordance with the literature. Risk of mortality increased with higher ASA score, male sex, and older age. Our study confirmed that comorbidities are found more often in patients who undergo delayed surgery[4,5] and that patients with a higher ASA score often wait longer for surgery[4,5,8,13,15] (Table I). Because we have no information about the reason for delay, a conclusion about the reason for this association cannot be made, but some delays might be due to preoperative optimization. The value of this often time-consuming optimization has been addressed by several previous studies, but further research is still warranted[24-27]. However, after adjusting for ASA score, we still found an association between surgical delay and risk of mortality, indicating that an increased risk of mortality with increasing surgical delay is present and is not exclusively due to decreasing medical fitness of the patients with longer delay times. Among the modifiable factors, we found no significant association between type of surgery and mortality, but did find one between the education level of the surgeon and mortality. The latter confirms previous findings by Khunda et al. that showed that the six-month mortality risk for patients with proximal femoral fractures increased when surgery was performed by a trainee without supervision[28]. As a consequence of this, several Danish orthopaedics departments have, in recent years, implemented polices stating that proximal femoral fracture surgery performed by interns and first and second-year residents must be supervised by an attending surgeon. However, this is only a hospital policy and does not currently have any legal implication. We are not aware of similar regulations in other countries. We propose that this topic be considered when making or updating guidelines in the future.

Previous studies have investigated the possible association between surgical delay and mortality. In a meta-analysis of fifty-two studies including 291,413 patients, Khan et al. found that the studies were too heterogeneous to allow for comparison and found no certain decrease in risk of mortality with reduced delay times but a decrease in postoperative complications[7]. The studies varied in sample size, inclusion and exclusion criteria, definition of delay time, number and types of factors taken into account when adjusting data, and follow-up time. Because the thirty-day mortality is used as an indicator by which departments are evaluated, we chose this as an end point for our study. Furthermore, ninety-day mortality was chosen as an end point to evaluate any development over time. We found that the effect of short surgical delay (less than twelve hours) in decreasing mortality was most pronounced at thirty days after surgery and that the effect was less (and not significant) at ninety days. To our knowledge, only two previous studies have investigated the effect of surgical delay of less than twelve hours. Uzoigwe et al. found a pronounced effect (an OR of 3.8 with surgical delay of more than twelve hours compared with less than twelve hours) for in-hospital mortality, and Smektala et al. found no significant adjusted effect on one-year mortality[6,11].

This might indicate that the effect of surgical delay of less than twelve hours is temporary and not as lasting as a surgical delay of less than forty-eight hours has been shown to be[29], but further research is needed.

The findings in this study strengthen the case for surgery earlier than the often-published forty-eight-hour limit, thereby supporting the recently established guidelines of surgery within thirty-six hours[2,30]. The recommendation of surgery within the same day or the next day after admission appears to be a compromise between surgery being performed as quickly as possible and being performed during the optimal hours by a skilled surgeon; the latter is also supported by this study. The beneficial effect of early surgery is often hypothesized to be caused by the reduced immobilization time, allowing faster rehabilitation and reducing risk of post-surgery complications such as respiratory infections, deep venous thrombosis, and decubitus ulcers[31-33]. The result would be a shorter hospital stay and a reduced risk of mortality. As more departments are expected to live up to this demand within the upcoming years, the main confounder of delay due to comorbidity is also expected to diminish. A continued evaluation of delay compared with mortality is therefore indicated.

In conclusion, a surgical delay of more than twelve hours significantly increased the adjusted risk of thirty-day mortality and a surgical delay of more than twenty-four hours significantly increased the adjusted risk of ninety-day mortality. The adjusted risk of both thirty-day and ninety-day mortality increased significantly when the education level of the surgeon was below that of an attending surgeon. The study findings challenge the departments to facilitate rapid surgical treatment supported by attending orthopaedic surgeons.

Appendix

eA The translated study protocol is available with the online version of this article as a data supplement at jbjs.org. ■

Note: The authors thank Alina Hansen, the administrative assistant of the Danish Fracture Database.

Anne Marie Nyholm, MD
Kirill Gromov, MD, PhD
Henrik Palm, MD
Thomas Kallemose, MSc
Anders Troelsen, MD
Department of Orthopaedic Surgery
(A.M.N., K.G., H.P., and A.T.) and
Clinical Research Centre (T.K.),
Copenhagen University Hospital Hvidovre,
Kettegaard Alle 30,
DK-2650 Hvidovre, Denmark.
E-mail address for A.M. Nyholm: rienyholm@gmail.com

Michael Brix, MD
Department of Orthopaedic Surgery,
Odense University Hospital,
Sønder Boulevard 29,
DK-5000 Odense C, Denmark

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