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Review

Timing in orthopaedic surgery – Rethinking traditional myths with a critical perspective

Jan Reinhard [b,1], Melanie Schindler [c,d,1], Josina Straub [a], Susanne Baertl [a], Dominik Szymski [a], Nike Walter [a], Siegmund Lang [a], Volker Alt [a], Markus Rupp [a,e,*]

[a] Department of Trauma Surgery, University Medical Center Regensburg, Regensburg, Germany
[b] Department of Orthopaedic Surgery, University Medical Center Regensburg, Bad Abbach, Germany
[c] Division of Orthopaedics and Traumatology, University Hospital Krems, Krems, Austria
[d] Karl Landsteiner University of Health Sciences, Krems, Austria
[e] Department of Trauma, Hand- and Reconstructive Surgery, University Hospital Giessen, Giessen, Germany

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ABSTRACT

Purpose: Standard operating procedures aim to achieve a standardized and assumedly high-quality therapy. However, in orthopaedic surgery, the aspect of temporal urgency is often based on surgical tradition and experience. At a time of evidence-based medicine, it is necessary to question these temporal guidelines. The following review will therefore address the most important temporal guidelines in orthopaedic surgery and discuss their practical relevance and potential need for optimization.
Methods: The systematic review features a literature review by database search in "PubMed" (https://pubmed.ncbi.nlm.nih.gov) for time to surgery in terms of (1) "proximal femoral fractures", (2) "femoral neck fractures", (3) "proximal humeral fractures", (4) "ligament and tendon injuries", (5) "spinal cord injuries", (6) "open fractures" and (7) "fracture-related infections". For every diagnosis, hypotheses on timing were set up and checked for evidence.
Results: There is solid clinical evidence supporting the initiation of treatment within 24 h for specific conditions like the surgical treatment of proximal femur fractures and prompt decompression of spinal cord injuries. However, for other scenarios such as the 6-hour rule for open fractures, joint-preserving femoral neck fractures, timing of ligament injuries, humeral head fractures and fracture-related infections there is currently no reliable evidence to guide prompt surgical treatment.
Conclusion: Based on the current data, resource-adapted surgical planning seems reasonable. Further research in these areas is necessary to determine the best timing of treatment and address existing doubts.

Purpose

Any medical intervention aims to ensure an early diagnosis and the best possible therapy for the patients. In surgical practice, guidelines for treating surgeons are of great importance. In clinical settings, standard operating procedures are developed for almost all possible diagnoses to achieve a standardized and assumedly high-quality therapy. The path taken here inevitably deviates from the ideal of an individual or today's often-promoted personalized therapy. The motives behind this are surely honourable and good, as the well-being of patients is the focus. Scientific progress, especially in recent decades, now allows important information to be available through high-quality prospective studies and numerous established registries, enabling the prescription and implementation of diagnostic and therapeutic steps into daily practice. However, in orthopaedic surgery, some qualitative aspects, especially regarding temporal urgency, are not yet clarified. These are partly based on surgical tradition and experience. Although this is of great importance in an empirical field like surgery, it is necessary to question

* Corresponding author at: Department of Trauma, Hand and Reconstructive Surgery, Rudolf-Buchheim-Strasse 7, 35385 Giessen, Germany.
E-mail addresses: jan.reinhard@ukr.de (J. Reinhard), schindler.melanie@gmx.at (M. Schindler), josina.straub@ukr.de (J. Straub), Susanne.baertl@ukr.de (S. Baertl), dominik.szymski@ukr.de (D. Szymski), nike.walter@ukr.de (N. Walter), siegmund.lang@ukr.de (S. Lang), volker.alt@ukr.de (V. Alt), markus.rupp@chiru.med.uni-giessen.de (M. Rupp).
[1] Shared first authorship. These authors contributed equally.

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temporal guidelines and shed light on their evidence. In times of increasingly scarce financial and personnel resources and already established financial sanctions such as in Germany where treatment is not reimbursed if a proximal femur fracture is not operated within 24 h [1], it is advisable to consider the significance of temporal guidelines for individual therapies. This can help individuals to adjust their own actions and therapy decisions sensibly for patients and collaborating staff as well as to assess potential other influencing factors for therapy success in relation to the factor of time. The following review will therefore address the most important temporal guidelines in orthopaedic surgery and discuss their practical relevance and potential need for optimization as orthopaedic surgeons encounter these in their daily clinical routine.

Methods

We performed a systematic review of the most important temporal guidelines in orthopaedic surgery. The literature review was conducted by database search in "PubMed" (https://pubmed.ncbi.nlm.nih.gov, accessed till 28th of February 2024). Database search was executed for time to surgery in terms of (1) "proximal femoral fractures", (2) "femoral neck fractures", (3) "proximal humeral fractures", (4) "ligament and tendon injuries", (5) "spinal cord injuries", (6) "open fractures" and (7) "fracture-related infection". In addition to each diagnosis the keywords "time to surgery", "timing", "early surgery", "late surgery", "time factor" were used. For every diagnosis, hypotheses on timing were set up and checked for evidence.

"Proximal femoral fractures need to be operated within 24 h to avoid higher mortality and complications"

Proximal femoral fractures demonstrate a relevant concern in orthopaedic practice, representing one of the most common types of fractures [2]. Current literature reports a one-year overall-mortality from 20 to 30 %, depending on the individual, pre-existing level of comorbidity [3–8].

Several studies confirm a direct correlation between mortality and complication rate and time to surgery, which refers to the duration between hospital admission and the time to surgery [4,9–14]. Different studies report increased mortality and complications if surgery was performed later than 24 h after admission to the hospital [12,13,15,16].

A Danish nationwide study involving 36,552 patients revealed that a delay in surgery of more than 24 h was associated with an elevated risk of mortality within one year, regardless of whether patients had comorbidities prior to the operation [15]. Patients suffering from a proximal femoral fracture but having oral anticoagulants (OACs) in their medical history often face delays in operative therapy and are reported to have higher mortality rates compared to those who do not take OACs [17,18]. According to recent literature, delaying surgery due to OACs intake is unjustified and concerns regarding the peri- and postoperative bleeding risk may be exaggerated [16,19–21].

Based on these findings various guidelines have been developed in different countries. Guidelines in the United States and Canada recommend prompt surgical therapy for proximal femoral fractures, ideally within 48 h of admission [12]. In Germany, guidelines established by the Federal Joint Committee require treatment of proximal femoral fractures within 24 h [1]. Accordingly, the U.K. recommends surgery within 36 h of admission [12].

Given the growing evidence, orthopaedic and trauma surgeons are beginning to implement a more refined strategy regarding the timing in the management of proximal femur fractures. Considering the literature and evidence, it is important to differentiate between 'time to surgery' and 'timing of surgery'. While 'time to surgery' refers to the actual duration from injury to surgical intervention and 'timing of surgery' pertains to the scheduling of the surgical procedure. Existing literature suggests that a delayed 'time to surgery' is associated with an increased risk of mortality and complications, regardless of the 'timing of surgery' [13]. There is an opportunity to optimize scheduling by extending proximal femur fracture operations into evenings and weekends. This strategic approach can help to reduce the time to surgery for proximal femur fractures, without compromising the scheduling of elective procedures.

"Closed reduction and internal fixation of femoral neck fracture has to be performed within six hours in joint preserving fracture care"

Internal fixation of femoral neck fractures is the optimum course of treatment for younger individuals under 60 years old as well as athletically demanding patients above 60 years without relevant comorbidities [22,23]. The precise function of time of surgery is less obvious, despite the universal agreement that the goals of treatment for these fractures should be anatomical reduction and stable internal fixation [24,25]. Non-union and avascular osteonecrosis are potential complications of femoral neck fractures [25–27]. Whether this fracture needs to be operated immediately, urgently, or the following day is still unclear based on the information currently available [25]. Early surgery can improve the blood supply of the femoral head due to immediate reduction of displaced femoral neck fractures and perform intracapsular decompression [25,28,29]. This assertion is based on the anatomical features of the blood supply to the femoral head, which makes it susceptible to traumatic vascular injury [27]. However, the femoral head's end connections are entirely intracapsular, they can be damaged by displaced femoral neck fractures, inadvertent fracture manipulation, or elevated intracapsular pressure [30]. Therefore, the nutrition of the femoral head is completely dependent on the artery of the ligamentum teres and the retinacular vessels, which may still be pervious [27]. The femoral head stays avascular, either totally or partially, at least for a while following a displaced femoral neck fracture [31]. For this reason, closed reduction and internal fixation of femoral neck fractures should be performed urgent [25,27]. However, to prevent a late segmental collapse of the femoral head, anatomical reduction and internal fixation of femoral neck fractures should also be performed as an urgent intervention [27]. The risk of femoral head osteonecrosis has been reported to be reduced by rapid reduction, which enhances and restores blood flow to the femoral head [26,32]. In contrast, a meta-analysis by Papakostidis et al. demonstrated no significant correlation between the time of internal fixation of a femoral neck fracture and the occurrence of avascular osteonecrosis [27]. However, an analysis of non-union cases suggests that the likelihood of non-union increases when internal fixation is delayed for longer than twenty-four hours [27]. Manninger et al. performed research on non-union and discovered that treating femoral neck fractures within six hours prevented non-union, whereas delaying surgery for more than 24 h the risk for non-union almost tripled, however, the degree of dislocation was not classified in this study [33]. The Garden classification is one of the various methods used for fracture classification. It categorizes fractures into four types: incomplete and valgus impacted (Type I), complete and nondisplaced (Type II), complete and partially displaced (Type III), and complete and fully displaced (Type IV) [34]. The risk of avascular osteonecrosis varies depending on factors such as the type of internal fixation, fracture type, Garden classification, preoperative traction, and time from injury to surgery [34,35]. Slobogean et al. reported a higher incidence of necrosis of the femoral head for displaced fractures (Garden III and IV types) of the femoral head than for undisplaced ones (14.7 % vs. 6.4 %) [36]. The same was observed by Parker et al. and Loizou et al. [37,38].

Some studies reported an increased rate of complications in case of delayed hip preserving surgical therapy more than 48 h [39–41]. In contrast, the subgroup analysis revealed no increased complications in case of total hip arthroplasty [39].

The outlined evidence makes it tough to lead to a conclusion regarding timing of surgical treatment. On the one hand, no significant correlation between the time of internal fixation of a femoral neck fracture and the occurrence of avascular osteonecrosis was found. On the other hand, closed reduction and internal fixation of the femoral neck should be performed as soon as the patient is stable and ready for anaesthesia. Immediate surgery allows for restoration of femoral head vascularization, early reduction, capsule decompression, anatomical reconstruction, and can reduce the risk of non-union [25,27]. However, one must take into consideration the higher rate of osteonecrosis in case of displaced fractures. Further studies can provide definitive clarity on the optimal timing of surgery.

"*Proximal humeral fracture – early fracture care avoids humeral head necrosis*"

Proximal humeral fractures represent up to ten percent of all adult human fractures [42,43]. Most frequently, this fracture occurs in elderly women resulting from low-energy trauma [44]. Posttraumatic avascular osteonecrosis results from traumatic interruption of the blood supply of the injured bone. The blood supply of the proximal humerus is mainly carried out by the anterior and posterior circumflex humeral artery, while the posterior branch supplies two-thirds of the humeral head [45,46]. According to recent literature, posttraumatic necrosis of the humeral head is reported in up to 34 % of patients [46]. Over the last years many studies investigated the hypothesis of a beneficial early fracture care in proximal humerus fractures. A single-centre study about risk factors for humeral head necrosis following open reduction and internal fixation in 154 patients showed that time to surgery did not influence the risk of humeral head necrosis [47]. This was also found in a retrospective cohort analysis which stated time to surgery to be neither protective nor a risk factor for osteonecrosis of the humeral head [48]. In a prospective study, Kloub et al. stated, that the outcome was neither influenced by delayed surgery nor by gender or age [49]. A recent systematic review and meta-analysis including 45 studies found no correlation between time to surgery and development of osteonecrosis of the humeral head [50]. In contrast, there is only one study involving 30 patients with fractures of the proximal humerus classified as B3 or C3. Here the patients were subdivided into groups based on the timing of surgery: early surgery ($\leq$48 h) and late surgery ($>$48 hour). It was found that after late surgery, all five patients developed avascular necrosis (AVN), resulting in a fivefold increased relative risk for AVN and subsequent associated surgical revision [51]. Instead of time to surgery, the type of fracture appears to be a risk factor for humeral head necrosis with higher risk of osteonecrosis in three- and four-part fractures according to Neer [47,48,52,53]. Additional risk factors for humeral head necrosis are smoking, bad reduction quality ($>$2mm dislocation) and disruption of the medial hinge with head extension less than 8 mm [47,48,50].

Based on the literature, early surgical treatment for a complex proximal humeral fracture can prevent humeral head necrosis. The timing of surgery may not present significant risk factors for proximal humeral fractures in simpler cases.

"*Early ligament and tendon repair results in better outcome*"

The incidence of ligament and tendon injuries is high. Regarding the shoulder, rotator cuff tears affect 34 % of all age groups and increase significantly with rising age [54]. Similarly, anterior cruciate ligament (ACL) tears are among the most prevalent types of football injuries across all levels of competition [55]. Achilles tendinopathy alone contributes to 7–11 % of all running injuries [56,57].

The timing at which ligaments and tendons need to be operated in orthopaedic surgery can vary based on several factors, including the specific type and severity, the location of the injury but also the overall health, and the choice of treatment [58]. While a direct repair through suture benefits from prompt treatment, in other circumstances surgery may be scheduled within a few days or weeks after the injury, allowing for swelling to subside, the technique of reconstruction (autograft, allograft, synthetic material) and the patient's overall condition to stabilize. Timely surgical intervention is crucial for younger, physically active patients experiencing acute tears and significant functional impairment [59]. Regarding operative therapy of traumatic rotator cuff injuries incorporating all different sizes, the outcome is not compromised for up to four months after the injury [60]. Tendon repair should be performed before tendon retraction and muscle atrophy develop [61]. Delayed surgical therapy after an unsuccessful period of physiotherapy can impact the outcomes of subsequent surgery [60]. A single randomized clinical trial, comparing early versus late surgical repair following unsuccessful nonoperative treatment, showed a tendency towards superior functional outcome after early repair without statistical significance [62]. Similarly in orthopaedic knee surgery and in particular ACL reconstruction, the perfect timing for orthopaedic surgery remains a matter of discussion [63]. In a recent meta-analysis, Shen et al. detected no significant superiority of early surgery regarding range of motion, knee laxity, and Tegener score. However, patients who received early ACL reconstruction showed significantly better results in the International Knee Documentation Committee (IKDC) and Lysholm score than delayed ACL. Early ACL varied from 8 days to 10 weeks, whereas delayed ACL was defined as occurring between 4 weeks and over 3 months [64]. Regarding the Achilles tendon, the comparison of direct suture and a delayed repair, even with a delay for up to four weeks, demonstrated similar functional results after one-year follow-up [65,66].

In conclusion, the myth of early repair being beneficial for ligament and tendon repair could not be proven in the literature. The literature does not definitively support the belief that early repair universally improves outcomes. Rather, the optimal timing can vary based on the specific injury, patient's overall health, and chosen treatment approach.

"*Spinal cord injuries have to be decompressed as soon as possible*"

Surgical intervention is essential in the acute phase of traumatic spinal cord injury (tSCI), aiming to realign and stabilize the spinal column and to decompress the spinal cord. The biological rationale behind early surgical decompression is to alleviate ongoing spinal cord compression that exacerbates ischemia and leads to secondary injury, suggesting that prompt intervention could confine the injury's extent and foster improved patient outcomes [67,68].

The variability in the timing of surgical interventions across the globe is notable, primarily due to the absence of definitive evidence, leading to a reliance on guidelines shaped by limited clinical data [69]. However, recent advancements have initiated a shift towards a consensus on the benefits of early decompression, ideally within 24 h [70]. Above all this current evolution is supported notably by the work of Michael Fehling's group, which evaluated data from 1548 patients across multiple, prospective, multicentre acute SCI databases, including the North American Clinical Trials Network (NACTN), SCI Registry, the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS), the Sygen trial, and the National Acute Spinal Cord Injury Study (NASCIS III) spanning from 1991 to 2017. Fehling's findings, capturing 1-year outcome data for 1031 patients indicated that patients undergoing surgical decompression within the first 24 h post-injury exhibit significantly better outcomes, including enhanced motor function, sensory recovery, and improved ASIA Impairment Scale (AIS) grades, especially in patients with cervical tSCI [70]. The study documents a decline in motor recovery benefits as the time to surgery extends, particularly noting a sharp decrease in efficacy after the first 24–36 h post-injury, thus highlighting a narrow therapeutic window for optimal intervention and coining the phrase "time is spine" [70]. However, practical challenges to implementing early decompression, such as patient stability, logistical issues comprising transportation, and infrastructural limitations, are significant [71]. A retrospective, monocentric analysis by Glennie et al. suggested, that practices may fall short, with only 62.0 % of SCI patients receiving surgery within the recommended 24-hour window in their cohort [71]. Nevertheless, it's critical to acknowledge that benefits still exist for surgeries conducted after this ideal period: Glennie et al. further demonstrated that while the most substantial improvements are linked with early intervention, delayed surgery can still provide meaningful benefits, advocating for the importance of not dismissing the potential for recovery with later interventions [71]. The ongoing debate on ultra-early decompression (within eight to twelve hours) [72,73] and on the role of interventions like expansile duroplasty or intrathecal catheter-based intraspinal pressure monitoring in targeted spinal cord perfusion management [74,75] continue to refine the understanding of optimal tSCI management.

"Open fractures have to be debrided within six hours to prevent infection"

The management of surgical wounds in open fractures is a topic of controversy. However, there is a general consensus that timely surgical intervention is crucial. The "6-hour rule," proposed by Friedrich in the 19th century, suggests that surgical debridement should be performed within the first six hours after trauma, as he observed a critical period for significant bacterial replication during this time [76]. This guideline was developed before the invention of antibiotics and are no longer relevant in the antibiotic era, which has been in place for the past 80 years. Despite numerous clinical studies attempting to validate this rule by exploring different time thresholds (such as five, eight, or twelve hours) for infection or non-union rates, conclusive evidence has been elusive [77–79].

However, both clinical and experimental data highlight the time-dependent increase in infection rates. Hull et al. found a three percent increased risk of infection for each hour of delay in surgical debridement in Gustilo-Anderson type II and III tibial fractures [80]. Additionally, Penn-Barwell et al. demonstrated that delayed surgical debridement and even more a delay in systemic antibiotic administration in an open fracture model in rats increased the risk of infection. Therefore, early antibiotic therapy and surgical debridement performed by an experienced team on a semi-elective basis within 24 h appears to be advantageous [81]. Early in 1989, Patzakis and Wilkins conducted one of the initial studies illustrating the absence of a connection between surgical timing and infection rates. Analysing 1100 patients with open fractures, they observed infection rates of 6.8 % and 7.1 % for fractures treated before and after twelve hours, respectively. Their findings highlighted that the primary factor contributing to infection reduction was the prompt administration of antibiotics [82]. In cases of compartment syndrome, limb devascularization, and significant contamination, immediate surgical intervention is imperative [83]. However, prompt treatment within a few hours remains preferable to surgical delay.

"Fracture-related infection should be treated as soon as possible"

The surgical treatment of fracture-related infections (FRI) incorporates confirming the diagnosis of FRI, identifying the causative organism, gaining local and systemic infection control, ensuring a healthy soft tissue envelope, and preventing chronic infection as well as implant or fracture instability [84]. Traditionally, it is still claimed that FRI should be treated as soon as possible, but there is a lack of evidence supporting this thesis, and current strategies are still based on recommendations. Indeed, urgent surgical intervention is essential in the presence of sepsis, severe systemic infection, rapid deterioration of local infection, and highly unstable fractures [85,86]. In all other cases, the management of FRI necessitates early surgical intervention for several reasons, irrespective of symptom onset [85]. Firstly, in the absence of clinical confirmatory criteria such as fistula, wound breakdown, or purulent drainage, the diagnosis relies on surgical sampling, emphasizing the need for early intervention [87].

Similar to open fractures, perioperative initiation of empirical antibiotic therapy followed by targeted antibiotic therapy seems to be beneficial for treatment outcome [88]. Therefore, intraoperative sampling of deep tissue samples is necessary to enable targeted antibiotic therapy, which is essential for treatment success and minimizing bacterial persistence [89,90].

Timely surgical intervention is also crucial to the outcome of treatment strategies, that basically consist of either implant retention or implant exchange in a single or multi-stage procedure. A key aspect in the pathogenesis of FRI is biofilm formation and the "race for the surface", which refers to the competition between bacterial colonization and host defence. As time passes since the onset of infection, the biofilm matures, making the bacteria up to 1000 times less sensitive to antibiotics [91]. In particular, if implant retention in terms of a DAIR approach (debridement, antibiotics, and implant retention) is intended, the time until revision surgery is crucial for treatment success. Thus, several studies have shown that success rates decrease from 100 to 86 % in early FRI (<3 weeks) to 82–89 % in a revision interval of three to ten weeks to 67 % in late FRI of more than ten weeks from onset of symptoms [92–96].

Early establishment of a healthy soft tissue envelope is vital for fracture healing, optimal antibiotic delivery, and preventing contamination, aligning with evidence suggesting that soft tissue defects in FRI are associated with less favourable outcomes [97]. No precise data on timeframes for soft tissue reconstruction is available for FRI, but a parallel can be drawn with open fractures. Therefore, early soft tissue coverage should be achieved within seven days to avoid increased risk of reinfection [98].

Finally, early achievement of fracture stability should be achieved to interrupt a vicious cycle in which interrupted neovascularization, osteolysis, and ongoing soft tissue trauma lead to further local inflammation as well as impaired local immune response and antibiotic penetration creating a supportive environment for bacteria [99].

In chronic and less dynamic FRI stages, close monitoring allows for early elective surgery, providing time for host and soft tissue optimization and careful surgical planning within a multidisciplinary and specialized team to gain the most favourable outcome for the individual patient [86,89,98]. This could also allow complex cases requiring multiple specialties to be referred to specialized centres, as is already partially established for the treatment of periprosthetic joint infections [100].

In summary, an "as soon as possible" emergent treatment of FRI is rarely required. In most cases, early but well-planned surgical treatment performed by a surgeon specialized in bone and joint infections should be sought. In contrast, in chronic but complex cases, host optimization followed by a timely but elective treatment conceptualized by a multidisciplinary team might be favourable.

Conclusion

There is solid clinical evidence supporting the initiation of treatment within 24 h for specific conditions like the surgical treatment of proximal femur fractures and prompt decompression of spinal cord injuries. In case of proximal femoral fractures, the existing literature suggests that a delayed 'time to surgery' is associated with an increased risk of mortality and complications. Therefore, operation should be performed as soon as possible. In terms of spinal cord injuries, different studies support early decompression, highlighting a narrow therapeutic window for optimal intervention and coining the phrase "time is spine".

However, for other scenarios such as the joint-preserving femoral neck fractures, humeral head fractures, timing of ligament injuries, 6-hours rule for open fractures, and fracture-related infections there is currently no reliable evidence to guide prompt surgical treatment. In case of femoral neck fractures, no significant correlation between the time of internal fixation and the occurrence of avascular osteonecrosis was found. On the other hand, closed reduction and internal fixation of the femoral neck should be performed as soon as the patient is stable and ready for anaesthesia. However, one must take into consideration the higher rate of osteonecrosis in case of displaced fractures. According to

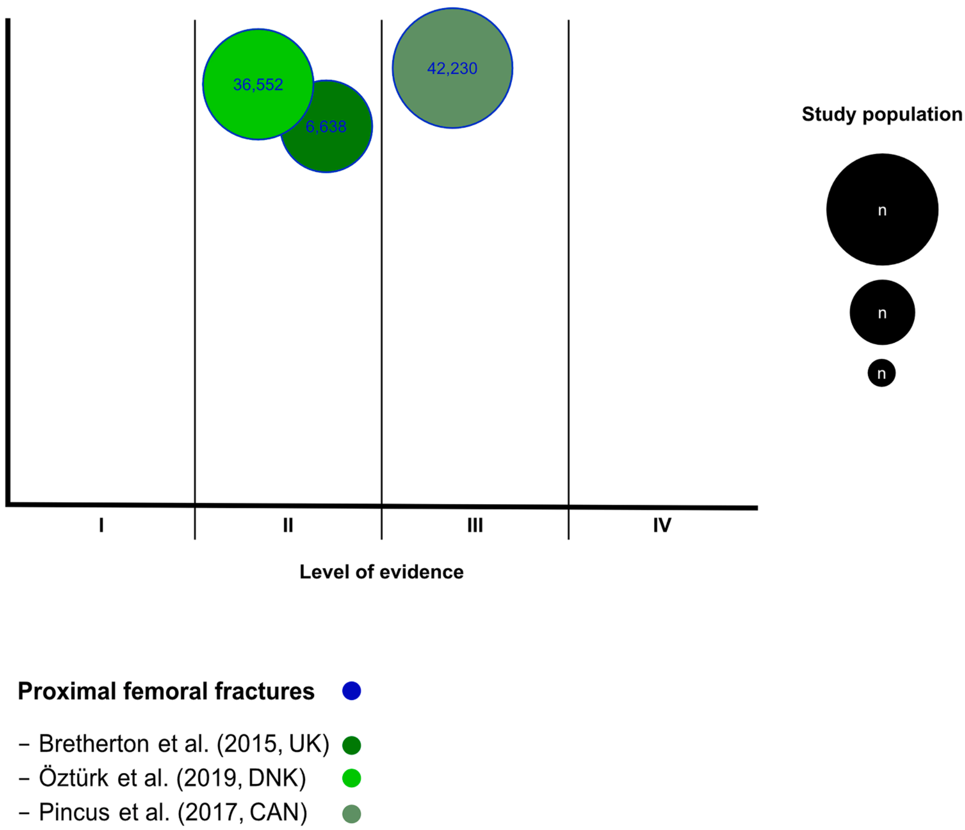

Fig. 1. Literature research on proximal femoral fractures regarding the timing for surgery. The studies are presented in regards on the study population and the level of evidence. "n" represents the number of included patients. The Y axis represents the seize of the study population, the X axis represents the level of evidence.

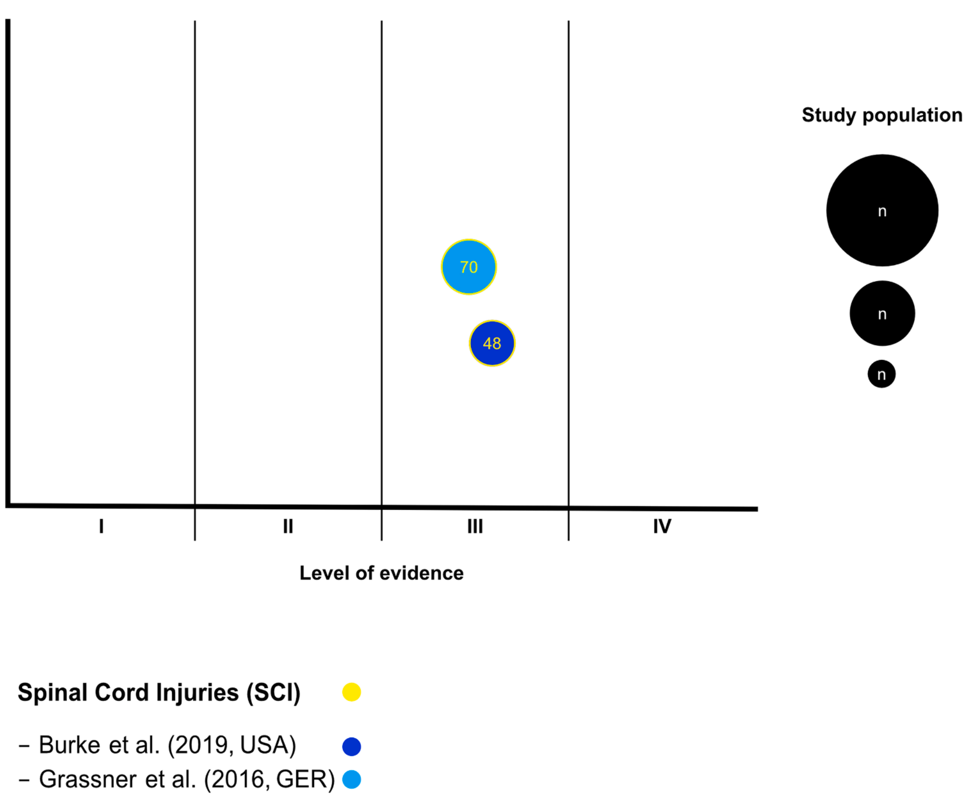

Fig. 2. Literature research on spinal cord injuries (SCI) regarding the timing for surgery. The studies are presented in regards on the study population and the level of evidence. "n" represents the number of included patients. The Y axis represents the seize of the study population, the X axis represents the level of evidence.

Table 1
Characteristics of the studies enrolled.

Author (year, country)	Patient number (time)	Age (mean)	Methods	Follow-up	Outcomes	Level of evidence	Study design
Proximal femoral fractures							
Bretherton (2015, UK)	6638 (1989–2013)	81.9	Association between time to surgery and mortality - Single-center study - time to surgery (hospital admission to surgery): 1–6 h, 7–12 h, 13–18 h, 19–24 h, 25–36 h, 37–48 h, 49–72h	30d	- Surgery ≤12 h improved survival-rate compared with surgery after 12h	II	Prospective
Öztürk (2019, DNK)	36,552 (2010–2015)	≥60	Association between time to surgery and mortality - Danish National Patient Registry - Surgery delay (hospital admission to surgery): >3h, >6h, >12h, >24 h, >48h	365d	- Surgery delay >24 h vs. ≤24 h showed higher 30d mortality in patients with medium level of comorbidity - Surgery delay was associated up to 45 % increased mortality in patients with none comorbidity - Surgery delay >24 h (vs. ≤24 h) and >48 h (vs. ≤48 h) was associated with higher 31–90d mortality	II	Prospective
Pincus (2017, CAN)	42,230 (2009–2014)	80.1	Association between time to surgery and 30d mortality - - Multi-center study (72 hospitals) - - early (≤24 h) vs. delayed surgery (>24 h)	365d	- delayed surgery (>24 h): higher risk for 30, 90, 365d mortality - delayed surgery (>24 h): higher risk for complications (pulmonary embolism, pneumonia, myocardial infarction)	III	Retrospective
Femoral neck fractures							
Kuner (1995, GER)	328 (1974–1987)	–	Femoral neck fractures in adults - Multi-center study (14 hospitals) - arly (≤24 h) vs. delayed surgery (>24 h)	46.7m	- best results early surgery (≤24 h) and use of dynamic hip screw	III	Retrospective
Jain (2002, CAN)	38	46.4	Comparison of early and delayed surgery in patients <60y - Single-center study - early (≤12 h) vs. delayed surgery (>12h)	24m	- no differences in functional scores - Delayed surgery: significant higher risk of avascular necrosis	III	Retrospective
Manninger (1989, HUN)	592	–	- Single-center study - Surgery at ≤6 h, 6–24 h, >24h	12m	- Delayed surgery >24 h triples risk of non-union	III	Retrospective
Proximal humeral fracture							
Boesmueller (2015, AUT)	154 (2005–2013)	55.8	Risk factors for humeral head necrosis and non-union - Single-center study - fracture of proximal humerus with head involvement (Type A n = 38, B n = 71, C n = 45)	>6m	- time to surgery did not influence risk for avascular necrosis or non-union	III	Retrospective
Da Silva (2022, GER)	305 (2008–2018)	61.5	Risk factors for humeral head necrosis - Single-center study - fracture of proximal humerus with head involvement (Type A n = 73, B n = 174, C n = 58)	476d	- time to surgery was neither a protective nor a risk factor for humerus head necrosis	III	Retrospective
Kloub (2019, CZE)	35	–	- Single-center study - two and three-part fractures of proximal humerus	256d	- 6x avascular necrosis, average time to surgery: 3.8d (range 1–18) - outcome was not influenced by age, gender or delayed surgery	II	Prospective
Schnetzke (2018, GER)	30 (2008–2014)	63	Rate of avascular necrosis after fracture dislocations - Single-center study - fracture of proximal humerus type B3 or C3 (AO) - early (≤48 h) and delayed surgery (>48 h)	37m	- early surgery (≤48 h) significantly decreases risk of acute vascular necrosis - delayed surgery (>48 h): all patients developed acute vascular necrosis	III	Retrospective
Ligament + tendon repair (shoulder)							
Mossmayer (2010, NOR)	103 (2004–2007)	60	Comparison between surgery and physiotherapy - Single-center study - Symptomatic traumatic or atraumatic small (<1 cm) or medium-sized (1–3 cm) rotator cuff tears	>12m	- Tendency towards superior functional outcome after early, versus late surgical repair after failed nonoperative treatment	I	Prospective RCT
Petersen (2011, USA)	36 (1992–2002)	57	Timing of rotator cuff repair - Single-center study - Variables: time (injury – repair), tear size, preoperative fat infiltration,	31m	- - No influence of tear size on patients outcome if surgery <4m - Worst outcome in patients with massive tears and surgery >4m	III	Retrospective

(continued on next page)

Table 1 (*continued*)

Author (year, country)	Patient number (time)	Age (mean)	Methods	Follow-up	Outcomes	Level of evidence	Study design
			patient satisfaction, improvement in pain				
Ligament + tendon repair (Achilles tendon)							
Maffulli (2020, ITA)	21 (2013–2016)	40	Timing of Achilles tendon repair - Single-center study - minimally invasive technique - early (<14d) and delayed (14–30d) surgery	12m	- similar results 1y postoperatively in early (<14d) and delayed (14–30d) surgery	III	Retrospective
Park (2017, KOR)	65 (2011–2015)	39	Timing of Achilles tendon repair - Single-center study - Surgery ≤24 h, 24–48 h, 48h-1w	3m	- no significant differences regarding isokinetic muscle strength and clinical outcome following surgery within 1 w after injury	II	Prospective
Spinal cord injuries							
Burke (2019, USA)	48	–	Time to surgery after Spinal cord injuries - Single-center study - ultra-early (<12 h), early (12–24 h), late surgery (>24 h)	–	- ultra-early surgery (>12h) showed significant better relative improvement in AIS grade	III	Retrospective
Grassner (2016, GER)	70	51	Time to surgery after Spinal cord injuries - Single-center study - Early surgery (<8 h) and delayed surgery (>8h)	12m	- - Early surgery (<8 h) showed significant higher Spinal cord independence measure difference (SCIM), better AIS grade and a higher AIS conversion rate - Early surgery (<8 h) showed significant better total motor performance	III	Retrospective
Open fractures							
Hull (2014, UK)	459 open fractures in 365 patients (2003–2007)	39.9	Association between delayed debridement and infection - Single-center study - Overall rate of infection 10 % (Grade II 6.9 %, Grade IIIa 10 %, Grade IIIb 20.5 %, Grade IIIc 19.2 % - mean time injury to debridement was 10.2h	12m	- Grade II + III injuries: significant increase in deep infections for each hour of delay (linear increase of 3 % per hour of delay) - No distinct time cut-off points were identified	III	Retrospective
Fracture-related infections (FRI)							
Kuehl (2019, CH)	229 (1999–2009)	55	Time-dependent differences in management of internal fixation-associated infections - Single-center study - Diagnosis (≥1): visible intraoperative purulence, sinus tract communicating with osteosynthesis, identical organism in ≥2x culture from intraoperative tissue/ sonication fluid, histological proof of inflammation - early (0–2 w after internal fixation), delayed (3–10 w), and late (>10w).	773d	- Staphylococcus aureus most prevalent (41.9 %) - Failure was observed in 11.7 % - Implant retention was highly successful in early and delayed infections but only limited in late infections	II	Prospective

* h = hours; d = days; w = week; m = months; cm = centimetre; AIS = Association Impairment Scale; SCIM = Spinal cord independence measure difference.

the recent literature, the complexity of proximal humeral fractures plays a major role in terms of humeral head necrosis. Especially in complex fractures, early surgical treatment can prevent humeral head necrosis. The myth of early repair being beneficial for ligament and tendon repair could not be proven in the literature. Rather, the optimal timing can vary based on the specific injury, patient's overall health, and chosen treatment approach. "Open fractures have to be debrided within six hours to prevent infection" appears to be a myth of the pre antibiotics era. The prompt administration of antibiotics seems to be the most relevant factor in these cases. In case of fracture related infections most studies recommend early but well-planned surgical treatment performed by a surgeon specialized in bone and joint infections. In these cases, emergency treatment is rarely required. Therefore, based on the current data, resource-adapted surgical planning seems reasonable. Further research in these areas is necessary to determine the best timing of treatment and address existing doubts. Fig. 1 and Fig. 2, Table 1

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CRediT authorship contribution statement

Jan Reinhard: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Investigation, Formal analysis, Data curation, Conceptualization. **Melanie Schindler:** Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **Josina Straub:** Writing – original draft, Formal analysis, Data curation. **Susanne Baertl:** Writing – original draft, Formal analysis, Data curation. **Dominik Szymski:** Writing – original draft, Formal analysis, Data curation. **Nike Walter:** Writing – original draft, Formal analysis, Data curation. **Siegmund Lang:** Writing – original draft, Formal analysis, Data curation. **Volker Alt:** Writing – original draft, Formal analysis, Data curation. **Markus Rupp:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Data availability

Data will be made available on request.

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