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"Tiers of Delay": Warfarin, Hip Fractures, and Target-Driven Care

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Abstract

Anticoagulation reversal is a common cause of operative delay. We sought to establish for the first time the impact this has on best practice tariff (BPT) for patients with hip fracture admitted on warfarin. All patients with hip fracture treated operatively over a 32-month period were reviewed. Basic demographics, time to theater, length of stay, and mortality were recorded for all patients. Independent samples *t*-tests were used to identify statistically significant differences between patients on warfarin and those not taking the drug. A total of 83 patients were admitted anticoagulated with a mean international normalized ratio of 2.65 and a median time to theater of 49.7 hours. Of these patients, 79% breached BPT, incurring significant financial loss. In the control group, 908 patients took a median 24.5 hours, a 28% breach of BPT ($P < .01$). Length of stay, Nottingham Hip Fracture Score, and predicted 30-day mortality were similar for both the groups. As well as affecting clinical outcome following hip fracture, delay due to anticoagulation causes considerable loss of BPT. Potential loss of revenue due to delays over the study period was £80 000, inspiring the establishment of an "early trigger" anticoagulation protocol. Although it is accepted that there are limitations to this work, it should raise awareness of the real impact of warfarin on patients with hip fracture both in terms of outcome and for the first time, loss of potential revenue.

Keywords

fragility fractures, geriatric trauma, systems of care, trauma surgery, basic research

Introduction

Management of a patient with a hip fracture is a key aspect of orthopedic trauma care, with around 75 000 new cases in the United Kingdom annually currently attracting a health care cost of £ 2 billion. With an aging population, the strain placed on hospital trauma services will continue to increase as by 2020; over 100 000 cases will be seen annually.[1] Any aspect of hip fracture management that optimizes both patient care and service provision therefore should be a focus of attention for clinicians and managers alike.

Delaying time to theater for operative intervention of hip fractures negatively impacts on patient outcome[2-6] and is one of the key aspects of the hip fracture best practice tariff (BPT). The BPT is part of a broader, payment by results process instigated by the UK Department of Health to adequately reimburse and incentivize high-quality and cost-effective care. The BPT program was introduced following the recommendations of Lord Darzi's 2008 High Quality Care for All report. This review of the National Health Service (NHS) identified 4 high-volume clinical areas where there was significant unexplained variation in practice: cataracts, fractured neck of femur, cholecystectomy, and stroke care. The BPT program is therefore one of the key enablers for the NHS to improve quality, by reducing unexplained variation and universalizing best practice.[7,8]

The BPT for hip fractures consists of 6 domains: surgery within 36 hours, admission under consultant-led joint orthopedic–geriatric care, admission using a multidisciplinary assessment protocol, review by a geriatrician within 72 hours, geriatrician-directed multiprofessional rehabilitation, and assessment for falls and bone protection. There is clear evidence of improved care in the population with hip fracture due to units meeting the hip fracture BPT criteria with significant benefit in patient outcomes.[9,10] In order to achieve the extra financial benefit (£1335 per patient) of the top-up payment that is additional to the base tariff received by the hospital for a hip fracture episode, all domains of the BPT (including operation within 36 hours)

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for hip fractures must be met. The data for each case are reconciled through the National Hip Fracture Database (NHFD).

One aspect of the perioperative management of patients with hip fractures that has been implicated in delayed operations is the use of maintenance dose warfarin for anticoagulation. Admission to hospital with a hip fracture while on warfarin with a significantly (>2.0) raised international normalized ratio (INR) has been associated with delay to theater and a trend toward greater mortality.[11] Pharmaceutical intervention leads to improved outcomes[12,13] and while a range of reversal agents are available, including oral vitamin K, the administration of low-dose intravenous vitamin K (IVK) has been shown in particular to expedite time to theater.[14] Evidence to guide agent choice and mode of delivery is disparate with both oral and intravenous administration of vitamin K between 0.5 and 10 mg being used routinely. With such huge discrepancy between reported dose ranges, clinicians are faced with choosing a protocol that balances efficacy and safety in addition to preventing prolonged periods of re-anticoagulation postoperatively.

Key to this situation is that regardless of the agent used, timing is crucial to ensure prompt reversal in order to allow patients to progress safely to the operating theater. An aggressive, prompt reversal policy to enable earlier surgery is recommended.[15]

Until recently, the existing hip fracture anticoagulation protocol within our unit was based on the often-conflicting evidence mentioned earlier. It involved administration of 1 mg IVK given following review of the patient with an INR > 1.5 by the admitting medical staff, following admission to the hip fracture ward from the emergency department (ED) as part of the "fast track" system.

In the United Kingdom, patients sustaining a hip fracture in the community are admitted to the ED on the hip fracture fast track, a nurse-led planned care package to streamline care and investigations in order to expedite operative management.

The use of a pathway in this manner enables coordination of analgesia, fluid resuscitation, appropriate imaging, and screening for significant concurrent medical pathology prior to expedited transfer to a dedicated hip fracture ward. Demonstrated to significantly reduce transfer times to orthopedic wards and streamline early hip fracture management, these systems allow a focus on the steps required to ensure prompt operative intervention, one of which is the reversal of anticoagulation.

As with any protocol of care, safety is an important feature and central to the hip fracture fast track is improving patient safety and outcomes. Although benefits in efficiency[16] and outcomes are proven,[17-20] care must still be taken to ensure that significant comorbidities are addressed, and while an emphasis on fast patient moving is beneficial, an awareness of the often significant comorbidities associated with this population is necessary. A report by Ollivere et al has highlighted the significant concurrent medical problems that may be inadequately addressed including concerns over suboptimal hydration in this population, leading to a suggestion that greater attention is paid to physiological parameters and "early warning systems" to be incorporated into fast track pathways.[21] In essence, a balance of fast track philosophy with a heightened awareness of comorbidities such as anticoagulation is required.[22] No follow-up of the anticoagulation regime specifically was in place in our department other than sporadic audit and data collection for the NHFD, which does not address delay through anticoagulation specifically. Anecdotal and rudimentary audit evidence suggested that compliance with the existing protocol was poor: dose, timing, and route of administration of IVK were variable, corroborating the experience of Tharmarajah et al, prior to the instigation of a new warfarin reversal policy.[13] As seen by Tharmarajah et al, despite the use of the existing but variably applied protocol, patients with hip fracture on warfarin were exposed to significant delay in time to theater. This has an impact both on the outcome of the patient and also in terms of the breach of BPT for hip fracture care.

It has been demonstrated that within the population with hip fracture on warfarin, pharmacological intervention decreases operative delay. No data exist however for the discrepancy in time to theater between patients with hip fracture on long-term warfarin and those not on the drug and the actual impact this has on the breach of BPT.

In order to establish these data, we carried out a study of the effect of long-term, maintenance warfarin administration on delay in time to theater and subsequent loss of BPT in patients with hip fracture at a University Teaching Hospital Major Trauma Centre.

Method

Following approval from the local audit committee, all consecutive admissions to the hip fracture unit at our institution over a 32-month period (April 2010-January 2013) were included in a retrospective assessment of a prospectively gathered database, generated to comply with data entry for the NHFD. Complete data were available for this period, as cases entered prior to this time had incomplete data points for key variables of components of the Nottingham Hip Fracture Score (NHFS).[23] Of note, the reason for delay in time to surgery is recorded by the hip fracture specialist nurse, where a breach occurs, thus identifying whether any breach was the result of factors other than the reversal of an elevated INR or whether BPT was not realized through failure in another domain.

All patients younger than 65 years of age, fractures sustained as a result of high-energy trauma, and those around an existing femoral prosthesis were excluded from analysis, as were hip fractures that were managed nonoperatively. Pathological fractures were included.

In addition to basic demographics, parameters noted included reason for warfarin prescription, length of stay, NHFS, and surgical intervention. Nonstratified parametric data analysis with independent samples *t*-tests identified statistically significant differences between patients with hip fracture admitted on maintenance warfarin for anticoagulation and a control group not taking the drug. The predicted 30-day mortality is calculated from the NHFS. Accepting the wide range of comorbidities associated with the population having hip fracture and the inability to perform meaningful regression analysis to the interdependence of the confounding variables, the NHFS is used as a surrogate marker for comorbidity and overall fitness.

Table 1. Comparison Data for Time to Theater, Patient Age, Length of Stay, NHFS, and Predicted Mortality for Both the Warfarin and the Control Groups.

	Time to theater, hours[a]		Age, years		LOS, days		Nottingham hip fracture score		Predicted 30-day mortality, %	
	Control (not on warfarin)	Warfarin	Control (not on warfarin)	Warfarin	Control (not on warfarin)	Warfarin	Control (not on warfarin)	Warfarin	Control (not on warfarin)	Warfarin
n	908	83	908	83	908	83	908	83	908	83
Average	32.09	53.71	81.21	82.08	16.09	16.67	4.45	4.71	6.78	7.02
St Dev	25.1	24.49	29.96	29.96	12.06	11.49	1.67	1.34	4.81	4.73
Mode	19.68	47.4	86	84	9	9	5	5	6.87	6.87

Abbreviation: LOS, length of stay; NHFS, Nottingham Hip Fracture Score; St Dev, standard deviation.
[a]$P < .001$.

Results

A total of 1024 (596 female and 428 male) patients with hip fractures were admitted over the study period of which 86 patients were taking warfarin on admission. Nonoperative management accounted for 3 patients in the warfarin group and 30 patients in the nonwarfarin control group. Following exclusion, there were 83 patients in the warfarin group and 908 in the control group. Of the patients, 53% sustained an intracapasular fracture and were managed by arthroplasty; the remainder were extracapsular fractures. Mean American Society of Anesthesiologists grade was 3 (1-4) for both the warfarin group and the nonwarfarin control group. There were no statistically significant differences seen in the age of the patients, their length of stay, their NHFS, or their predicted 30-day mortality. A highly statistically significant difference was seen in the time to theater between the warfarin group and the control group (Table 1).

Within the warfarin group, the mean INR was 2.65 (1.10-6.00), and 80 of the 83 patients had an INR of >1.5. Mean number of preoperative INR samples taken was 3 (2-6). The mean pretheater INR was 1.45 (1.0-1.9) and 16 of 83 had INR >1.5 at theater. Of the 83 patients, 3 had a metallic heart valve and were commenced on an individual patient basis on bridging low-molecular-weight heparin following review by a cardiologist. The remaining 80 patients were on warfarin for arrhythmia (58 patients: 40 with atrial fibrillation and 18 with other arrhythmias) or previous thromboembolic event (22 patients: 14 with previous ultrasound scan proven deep vein thrombosis and 8 with previous pulmonary embolus).

In terms of BPT, 28% (257 of 908) of nonwarfarinized patients breach the 36-hour window on time to theater in contrast to 79% (66 of 83) in the warfarin group. There was no difference between patients admitted in daylight hours (0800-1600) and patients admitted out with this time in terms of time to theater. From the prospectively collected data in which exact reasons for breaching are recorded, none of the patients within this cohort breached for any other reason other than the reversal of their elevated INR.

Discussion

The BPT for hip fracture care was introduced due to the volume of cases and the clear evidence that prompt surgical intervention, among other factors, improves patient care in this often complicated, vulnerable group. Financial incentives now exist for orthopedic departments to prioritize the care of hip fractures and central to this is ensuring that all hip fractures proceed to the operating theater, if indicated, with minimal delay. Published guidelines recommend surgery on the day of, or day after, admission.[8] Although it is known that warfarin causes delays to theater, our data reveal for the first time since the instigation of tariff-based remuneration, the extent of these delays, and the significant financial differences that exist between the 2 populations.

There are a number of system and human factors that contribute to delays in patients with hip fracture. Despite the existence of a fast track system, the time patients spend in the ED is still considerable. Our institution achieves admission to the ward from arrival at the ED in 2.9 hours although at a national level, the mean time to admission to an orthopedic ward for the patient with hip fracture is 9.2 hours.

For patients admitted on a maintenance dose warfarin for anticoagulation, the hip fracture warfarin reversal protocol is initiated on review by the ward doctor based on the results of the INR sample taken in the ED, dependent on receipt of a satisfactory sample. Delays of several hours can occur between admission to the ED, review on the ward, and prescription of vitamin K. Again receipt of vitamin K is not immediate following prescription, and further delays in drug administration can occur.

Delays are inherent with warfarin reversal, and a reversal window is unavoidable. The pharmacokinetics of IVK administration demonstrate a predictable bioavailability and while the peak reversal effect is seen at 24 hours, significant decreases in INR will be seen after 6 to 12 hours, particularly in patients who are excessively anticoagulated.[24] Although it has been common practice in our unit and others in the United Kingdom to check the INR after 6 hours from IVK administration, this timing is often erratic, may well occur prior to 6 hours and regardless is almost certainly too early following IVK administration to obtain a realistic reversal. In this study, the majority of patients had at least 3 preoperative INR samples taken due to the timelines of the existing protocol.

This illustrates the extent of delays inherent within this population and represents a further logistical and financial burden associated with untimely or inadequate reversal.

Warfarinized patients thus present a predictable challenge to prompt operative management, as reversal to an INR of <1.5 is sought by anesthetic and surgical teams. For each window following the administration of vitamin K prior to assessment of the clotting profile, the likelihood of early surgery diminishes. Audit performed within our department of delays in the administration of vitamin K for warfarinized patients has suggested that the system and human factors inherent within the current protocol result in a minimum delay of 6 hours from arrival at the ED to the administration of the first dose of vitamin K. Having already lost a considerable quantity of their allotted preoperative window, these patients may often require further administration of vitamin K and a further INR check.

Key to improving the management of these patients which we have clearly identified as having a predictable, significant impact on delay to theater is an early "trigger" to the administration of vitamin K. In order to negate the impact of the "tiers of delay," we have instigated the administration of 2 mg IVK to be given in the ED to all patients on warfarin once a hip fracture is confirmed, prior to the availability of an INR result.

As detailed previously, choosing an administration route and dosing schedule is not assisted by literature review due to the hugely disparate reports used by a number of units. We were guided by the work of Tharmarajah et al using low-dose IVK with no reported complications.[13] In this work, they detail the use of 1 mg IVK although the time to surgery in this intervention group remained high at 67 hours. There is no record in the literature regarding the ideal timing of administration and all reports base the administration of IVK only with a known INR result. Following discussion with hematology staff and review of the literature, an agreed protocol of administration of 2 mg IVK prior to knowledge of an INR was decided.

Clearly, a full assessment of the patient is made prior to administering the IVK with corroboration of warfarin prescription taken from the existing hospital notes, the notes from the patient's institutional residence, or the community physicians' prescription that is brought in with the patient to the ED. Our data demonstrate that in 80 of 83 patients, reversal was required and similarly, in all but 3 patients, "low-risk" indications for anticoagulation were seen.

It is unlikely therefore that reversal would either not be required or would be harmful if performed. It is acknowledged that even accepting that reversal was indicated in nearly all patients and in addition none of the patients had any thromboembolic complications, concerns exist regarding the broad use of IVK in this manner. The 3 patients with metallic heart valves were seen by a cardiologist preoperatively and bridging low-molecular-weight heparin was commenced. Numerous regimes are available for bridging therapy and many are hospital specific; the evidence on which these regimes are founded is however well established.[25-27]

Due in part to the implications of delaying surgery and the obvious requirement to efficiently manage hip fractures due to the growing burden of fragility injuries, there is now a wealth of evidence regarding the issue of anticoagulation management in this population. There is firm evidence both for the requirement of protocols in hip fracture care, the morbidity associated with delays to theater in patients with hip fracture on warfarin, and the benefits of IVK administration.[11,12,14,15,28-31]

In particular, Leonidou et al found that IVK administration resulted in not only a decreased delay to theater but also the lowest rate of complications.[30] It is appropriate that any broad protocol-driven path of care should be met with a degree of concern, but for the early administration of IVK in the warfarinized population with hip fracture, the wealth of evidence supports its safe and beneficial use.

With an increasingly aging population, which is now the subject of financial incentives, hip fracture management will continue to dominate orthopedic departments across the United Kingdom. Within our unit, the loss of BPT in the warfarin group over the study period equates to a loss of revenue of £80 000. It is acknowledged that this work is limited by an absence of stratification and the heterogeneity of the study groups. Regression analysis would be required to more robustly attribute these delays and the loss of revenue entirely to warfarin although the extent of the delay, the group size, and the prospectively collected reason for breach strongly suggest that warfarin is the main factor in causing these patients to wait for surgery. Similarly, although a new protocol has been instigated, its impact is as yet unreported although every patient admitted on warfarin under the new protocol has achieved operative intervention within 36 hours. Interim analysis and further data collection following integration of the new anticoagulation reversal protocol will be reported in due course.

These limitations notwithstanding, it is recommended that in the light of the findings of this study, orthopedic surgeons as part of the multidisciplinary hip fracture care team should evaluate the impact of warfarin on their patients and look to instigate earlier "protocol triggers" to warfarin reversal prior to assessment of the admission INR result. As stated earlier, some delays are inherent when managing patients with hip fracture admitted on warfarin due to the requirement for a "reversal window." The key point of this work and what will impact on patients and clinicians in light of the BPT is how best to manage the reversal window and to prevent it from resulting in unnecessary exacerbation of an existing delay.

The measures that clinicians can take to minimize these predictable, unnecessary delays are:

- Early-triggered IVK without knowledge of the INR—this ensures that the necessary reversal window starts as early as possible in the ED;
- Instigating the culture of corporate responsibility for the early management of patients with hip fracture on warfarin. Multidisciplinary focus on the reversal window and the timely and accurate handover of timelines for INR checks.
- Checking INR levels at 12 hours instead of 6 hours following administration of IVK—this will afford an increased chance of reversal to be confirmed per the

pharmacodynamics of IVK as discussed earlier. Testing at 12 hours reduces the number of samples required preoperatively and confirms the benefit of early-triggered IVK administration—the earlier the IVK is given, the earlier in the patient admission that the 12 hours check is done.

- ''Near patient'' testing: nurse-administered bedside testing of venous coagulation samples using a portable machine—not currently a feature of our department but will form an evolution of our protocol. Bedside INR testing will further reduce delays in blood sample processing and resultant IVK prescription where required, reinforcing near-patient care.

By negating the ''tiers of delay'' evident in anticoagulation reversal in these patients through these measures, improved outcomes and compliance with BPT should be achievable.

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