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Abstract

Aims

We compared implant and patient survival following intraoperative periprosthetic femoral fractures (IOPFF) during primary total hip arthroplasty (THA) with matched controls.

Methods

This retrospective cohort study compared 4831 hips with IOPFF and 48154 propensity score matched primary THAs without IOPFF implanted between 2004 and 2016. Implant and patient survival rates were compared between groups using Cox regression.

Results

10-year stem survival was worse in the IOPFF group ($p < 0.001$). Risk of revision for aseptic loosening increased 7.2 fold following shaft fracture and almost 2.8 fold after trochanteric fracture ($p < 0.001$). Risk of periprosthetic fracture of the femur revision increased 4.3 fold following calcar-crack and 3.6 fold after trochanteric fracture ($p < 0.01$). Risk of instability revision was 3.6 fold after trochanteric fracture and 2.4 fold after calcar crack ($p < 0.001$). Risk of 90-day mortality following IOPFF without revision was 1.7 fold and 4.0 fold after IOPFF with early revision surgery versus uncomplicated THA ($p < 0.001$).

Conclusions

IOPFF increases risk of stem revision and mortality up to 10 years following surgery. The risk of revision depends on IOPFF subtype and mortality risk increases with subsequent revision surgery. Surgeons should carefully diagnose and treat IOPFF to minimise fracture progression and implant failure.

- IOPFF increases risk of stem revision and mortality up to 10-years following surgery.
- The risk of revision depends on IOPFF subtype and mortality risk increases with subsequent revision surgery.

Introduction:

Total hip arthroplasty (THA) is a highly successful procedure with a low complication rate. One significant complication is intraoperative periprosthetic femoral fracture (IOPFF). IOPFF can occur in the trochanteric region, calcar or femoral diaphysis¹. The incidence of IOPFF in primary THA ranges from 1–5%²⁻⁴. Most IOPFF occur during canal preparation and stem implantation², when the circumferential strains of the proximal femur are highest⁵, especially when the surgeon establishes implant stability through press-fit fixation with cementless implants⁶. Treatment of IOPFF is specific to fracture type and stability⁷. Calcar cracks are commonly treated with cerclage wires or cables^{8,9}, shaft fractures with internal fixation and/or revision to a distally fixed stem² and unstable trochanteric fractures with wiring or plating^{2,10}.

Case series have reported excellent outcomes with appropriately treated IOPFF^{11,12}. More recently however, IOPFF has been linked to an increased risk of post-operative periprosthetic femoral fracture (PFF) and higher revision risk^{2,8,13,14}. Any revision surgery also increases 30-day and 90-day mortality¹⁵, but the specific effect of IOPFF on mortality has not yet been estimated.

The purpose of this study was to estimate implant and patient survival rates following IOPFF compared to a matched cohort of patients undergoing uncomplicated primary THA using data from the National Joint Registry (NJR) for England and Wales, the world's largest joint registry.

Materials and Methods:

Dataset:

The NJR records patient and surgical data for all THAs performed at hospitals in England and Wales since 2003; with overall missing data estimated at 5.8%¹⁶. Surgeon-reported IOPFF, have been collected since 1st April 2004. This study investigated all primary stemmed THAs in the NJR from 1st April 2004 to 30th September 2016.

Participants

793976 THAs were eligible for analysis. Exclusions were; missing follow-up data (n = 15), cases from the Isle of Man (low numbers, n= 153) and where the bearing type was not a combination of metal on polyethylene (MoP), ceramic on polyethylene (CoP), ceramic on ceramic (CoC) or metal on metal (MoM) (n = 12 566). The resulting subset of data included 781 242 primary THAs.

Institutional ethical approval was granted for this study.

Variables

All variables relating to patient age, sex, ASA grade (1-2 vs 3-5), year of surgery, side, surgical approach (anterolateral [Hardinge, anterolateral and lateral], trochanteric osteotomy, posterior, other), computer guided surgery, minimally invasive surgery, surgeon grade (consultant/non-consultant), hospital type, indication, stem fixation type, bearing combination and type of thromboprophylaxis were included. We included IOPFF reported as either “calcar crack”, “shaft fracture”, “shaft penetration”, “trochanteric fracture” and text describing IOPFF in “other”. Cases were grouped as calcar, trochanter or shaft fractures.

Outcomes

The primary outcomes were implant survival and patient survival. Implant survival was estimated until stem-only revision (all stem attributable revisions: Aseptic stem loosening [ASL], instability, PFF, pain, infection, stem fracture, stem malalignment) and separately for revisions indicated for PFF, instability, ASL and infection. Implants which were not revised during follow up were censored. Patient survival was estimated from primary surgery until death using pre-existing NJR data from the Office for National Statistics database, which provides data on all-cause patient mortality, using unique patient identifiers.

Statistical analysis:

Comparisons of continuous variables were performed with two-way analysis of variance for non-normally distributed data, and categorical variables were compared with chi-square tests. Since the dataset was large and multiple comparisons were made, a significance level of $p < 0.01$ was chosen.

The proportional hazards assumptions were satisfied for all analyses. All analyses were performed using R (V 3.5.1, Vienna, Austria).

Influence of IOPFF on implant survival

Propensity scores were used to match patients who sustained IOPFF (IOPFF group) to similar patients without IOPFF (Control group) at a ratio of 1:10 with a 0.04 standard deviation calliper matching width. Propensity scores were generated using logistic regression and represented the probability that a patient sustained IOPFF during primary THA. Variables used for matching were selected using a previously established model and included: age, gender, ASA grade, diagnosis, side of surgery, lead surgeon grade, organisation type, computer guided surgery, approach, stem fixation and bearing combination. Adequate balance of the IOPFF vs control group was assumed when the standardized mean difference (SMD) was <10% for each variable. Implant survival at up to 10-years was estimated using the Kaplan-Meier method and survival difference between IOPFF and controls was assessed using a log-rank test. Estimation of implant survival was assessed for each revision indication. Kaplan-Meier plots were assessed visually to identify the time period in which a difference in revision rate occurred between IOPFF and controls. The influence of IOPFF on implant survival during this period was assessed using univariate Cox regression models to estimate the adjusted hazard ratio with 95% confidence interval (HR [95%CI]) of revision for those with IOPFF compared to controls. Multivariable regression was utilised for subtypes of IOPFF, which were adjusted for age, gender, ASA score, indication for surgery, bearing combination and stem fixation to reduce confounding error.

Influence of IOPFF on patient survival

Unadjusted patient survival was estimated up to 10 years using the Kaplan-Meier method and compared between IOPFF and no IOPFF groups using a log-rank test. Cases were coded according to whether the patient has an IOPFF and subsequent revision. Multivariable Cox regression models were used to assess the influence of IOPFF on mortality, which were adjusted for age, gender, ASA score, indication for surgery, bearing combination, approach, stem fixation and thromboprophylaxis¹⁷.

Results:

Following exclusions the overall prevalence of IOPFF was 0.62% (4833/781 242). The prevalence of IOPFF during cemented stem implantation was 0.87% (2969/ 341 115) for cementless stems and 0.42% (1864/ 440 127). Only two cases in the IOPFF group could not be appropriately matched. Matching was achieved at a ratio of close to 1:10 within the parameters of the matching algorithm. Matching resulted in 4831 hips in the IOPFF group and 48154 hips in the control group. Good balance between IOPFF and control groups was achieved (SMD <8.3%, table 1). Median (IQR) follow-up time in IOPFF and control groups were similar (5.4 years [3.2 - 8.1] versus 5.5 years [3.2 - 8.3], p=0.305). Follow up ranged from 0.0 to 13.9 years in both groups. In the IOPFF group the prevalence of stem only revision in the five-years following THA was significantly higher than in the control group (3.01% versus 2.01%, p<0.001).

Influence of IOPFF on implant survival

Ten-year implant survival for stem revision was significantly worse in the IOPFF group compared to controls (95.4% [94.5 – 96.2] versus 96.8% [96.6 – 97.1], $p < 0.001$). The survival difference between IOPFF and controls became apparent within the first 6 months and gradually increased up to ten years (figure 1). Relative hazard of stem revision in the first six months due to IOPFF versus no IOPFF was 2.6 (CI 2.0 – 3.4, $p < 0.001$). Adjusted risk of stem revision within six months versus no IOPFF was greatest with trochanteric fracture (HR = 3.0 [CI 1.9 – 4.8], $p < 0.001$) followed by shaft fracture (HR = 2.9 [CI 1.2 – 7.1], $p = 0.018$) and calcar crack (HR = 2.4 [CI 1.7 – 3.3], $p < 0.001$) (figure 6).

Ten-year implant survival until revision for ASL was significantly worse in the IOPFF group compared to controls (99.0% [CI 98.7 – 99.4] versus 99.3% (99.2 – 99.4), $p = 0.004$). The implant survival difference between IOPFF and controls became apparent within the first six months and steadily increased to five years (figure 2). Risk of revision in the first five years for aseptic loosening associated with any IOPFF versus no IOPFF was 2.1 fold (HR 2.1 [CI 1.3 – 3.2] $p = 0.001$). The adjusted risk of stem revision for ASL within five years versus no IOPFF was greatest following shaft fracture (HR 7.2 [CI 2.9 – 17.7], $p < 0.001$) followed by trochanteric fracture (HR 2.8 [CI 1.3 – 5.9], $p = 0.01$) and least likely post calcar crack (HR 1.5 [CI 0.8 – 2.7], $p = 0.200$) (figure 6).

Ten-year implant survival until stem revision for PFF was significantly worse in the IOPFF group compared to controls (98.8% [98.4 – 99.2] versus 99.4% [99.3 – 99.5], $p < 0.001$). The survival difference between IOPFF and controls became apparent within the first 6 months and maintained a similar trend up to ten years (figure 3). Hazard ratio of revision for PFF over 6 months for any IOPFF versus no IOPFF was 4.2% (CI 2.7 – 6.5, $p < 0.001$). The adjusted HR of revision within 6 months for PFF versus no IOPFF was greatest following shaft fracture (HR 4.4 [CI 1.1 – 18.1], $p < 0.039$) then calcar crack (HR 4.3 [2.6 – 7.2], $p < 0.001$) and finally trochanteric fracture (HR 3.6 [CI 1.6 – 8.3], $p = 0.003$) (figure 6).

Ten-year implant survival for revision for instability was significantly worse in the IOPFF group compared to controls (98.7% (CI 98.3 – 99.2) versus 99.2% (99.1- 99.3), $p < 0.001$). The survival difference between IOPFF and controls became apparent within the first 6 months and maintained a similar trend subsequently, up to ten years (figure 4). Risk of revision for instability associated with IOPFF versus no IOPFF within 6 months was almost three-fold (HR 2.7 [CI 1.8 – 4.2] $p < 0.001$).

Adjusted risk of revision for instability versus no IOPFF within 6 months was greatest with trochanteric fractures (HR 3.6 [CI 1.8 – 6.9], $p < 0.001$) then calcar cracks (HR 2.4 [CI 1.4 – 4.2], $p = 0.001$) and then shaft fractures (HR 1.5 [CI 0.2 – 10.7], $p = 0.690$) (figure 6).

Ten-year implant survival for revision for infection was not significantly different in the IOPFF group compared to controls (99.2% (CI 98.8 – 99.6) versus 99.4% (99.3- 99.5), $p < 0.20$) (figure 5). Risk of revision for instability associated with IOPFF versus no IOPFF was not statistically significant over the ten year period (HR 1.3 [CI 0.9 – 2.0] $p = 0.184$). Adjusted risk of revision for instability versus no IOPFF over ten years was not statistically significant for calcar cracks (HR 1.3 [CI 0.8 – 2.1], $p = 0.37$), shaft fractures (HR 3.0 [CI 0.0 – infinite], $p = 0.99$) or trochanteric fractures (HR 1.7 [CI 0.9 – 3.2], $p = 0.11$) (figure 6).

Influence of IOPFF on patient survival

Unadjusted six month patient mortality was 1.7% for patients with IOPFF and 0.9% for patients without IOPFF. Unadjusted ten-year patient mortality was also significantly worse in the IOPFF group compared to controls (29.9% [CI 27.0 – 30.8] versus 25.7% [CI 25.1 – 26.3], $p < 0.001$). The survival difference between IOPFF and controls became apparent within the first 6 months and very slowly increased up to ten years (figure 7).

Estimated hazard of mortality during first six months post-operatively associated with IOPFF versus no IOPFF was 1.8 (CI 1.4 – 2.2, $p < 0.001$). The adjusted HR of death within 90 days for patients with IOPFF who did not go onto revision versus patients with no IOPFF or revision surgery was 1.7 (CI 1.3 – 2.2, $p < 0.001$). The adjusted risk of death within 90 days for patients with IOPFF who went onto revision within 90 days versus patients with no IOPFF and no revision surgery was 4.0 (CI 1.5 – 10.5, $p < 0.001$).

Discussion:

This is the largest study assessing patient and implant survival following intra-operative femoral fracture sustained during primary THA. Patients with IOPFF incur a higher risk of revision compared to those without IOPFF and the risk of revision is related to the specific IOPFF subtype. Patients with IOPFF have almost double the risk of death at six months, compared to those without IOPFF. Patients who require early revision following IOPFF have a four-fold risk of dying within 90 days.

IOPFF and stem survival

Stem survival was worse for all possible revision end points with the exception of revision for infection following IOPFF compared to matched controls. The risk of all revision was 2.6 times the risk of controls for all cause stem revision, which is similar to other studies¹⁴. IOPFF increased the risk of early revision for all causes and specifically for PFF, aseptic loosening and instability.

Thillemann found that the risk of unspecified IOPFF which underwent intraoperative fixation had a seven-fold relative risk of revision for instability during the initial six-month period¹⁴. We found that the relative risk of revision for instability was four-fold higher with IOPFF. The risk was highest following trochanteric and calcar fractures. Trochanteric fractures can lead to reduced function of the hip muscles, stem subsidence and loss of stem version¹⁸. Calcar fractures may compromise the primary stability during surgery leading to stem subsidence over time which may slacken periarticular structures and lead to instability^{19, 20}.

IOPFF have previously been linked to increased risk of revision for periprosthetic fracture^{9, 14}. In this study, IOPFF led to significantly worse ten-year implant survival and a greater than 3.5 fold increase in the risk of PFF revision within the first six months. The greatest risk was following calcar crack, which increased the risk of PFF revision within six months by over four-fold. Early PFF revision may be the result of fixation failure with fracture propagation due to either physiological loading or a new injury. Calcar crack has previously been suggested to be an innocuous injury when treated appropriately^{8, 21}. The true extent of calcar cracks can be difficult to fully identify during primary surgery, which may lead to inappropriate internal fixation. This may be due to reluctance to expose the proximal femur fully and difficulty identifying fractures on intraoperative radiographs because there is no fracture separation when the implant is removed or the femur is difficult to assess when a rasp or implant remains implanted. Use of plastic stem replicas intraoperatively may make the full extent of calcar fractures more obvious on intraoperative radiographs.

IOPFF was associated with a significantly worse 10-year ASL revision rate. Unsurprisingly, shaft fracture increased the risk of ASL revision seven-fold, probably because of the reduced ability of the surgeon to generate adequate fracture stability to withstand large hoop stresses generated by cementless and cemented implants, loss of stability may lead to failure of osseointegration in

cementless implants and loss of mantle integrity around cemented implants. Current guidance advocates the use of a distally fixed stem when adequate proximal fixation is not achieved¹⁰. It is not possible from this study to ascertain whether such guidance was implemented. Interestingly calcar cracks did not lead to a significantly increased risk of five year ASL revision. This suggests that calcar cracks which are not revised for other causes do not lead to long term implant. It may be that cases with calcar cracks are more likely to be revised for PFF revision within the first few months rather than ASL at a later date. Trochanteric IOPFF were associated with an almost three-fold increase in risk of five year ASL revision. Hip muscle dysfunction may increase the resultant peak contact forces and joint reaction force measured in implanted femoral stems²³, increasing the stress on the implant-bone interface and the likelihood of failure. Trochanteric fractures may also reduce proximal stability if the trochanteric fracture fragment includes a part of the distal metaphysis which may normally stabilise the upper stem body.

This study did not show any difference in rates of revision for infection between patients sustaining an IOPFF and matched controls. This is surprising given the expected increase in operating time that might be expected following an IOPFF, which has previously been linked to an increased risk of infection²³. A failure to demonstrate any difference in rates of infections between groups may be due to a lack of adequate controls in this observational study which prevent matching on other important factors such as antibiotic prophylaxis.

Patient survival following IOPFF

Patient survival in the IOPFF group was significantly worse up to 10-years after primary surgery. The difference in survival was evident most markedly within the first six months post-operatively, where the risk of dying within 6 months increased almost two-fold for any IOPFF when adjusting for all other available factors¹⁷. When modelling the interaction of IOPFF and subsequent revision surgery within six months, patients with IOPFF and no stem revision surgery had double the risk of dying versus those without IOPFF or revision surgery. This demonstrates that part of the excess mortality may come from the IOPFF as a result of increased blood loss, prolonged surgery, reduced mobility and longer hospital stay. Part of the excess mortality in the IOPFF group may be due to increased revision burden since patients who had IOPFF and subsequent stem revision had a four-fold increased risk of dying versus no IOPFF or revision in the first six months.

Limitations

Whilst registry data is crucial to the investigation of outcomes following uncommon complications the results show association between recorded variables and observed outcomes and do not necessarily represent causation. Confirmation of causation should be sought using the breadth of good

clinical research findings. THA is very successful and further advances are likely to take the form of small incremental changes. Despite this, large numbers included in this study increased statistical power and may have led to results which are statistically significant but do not reach a levels of clinical significance and as such should be viewed within the overall clinical context by experienced clinicians. The NJR records self-reported intraoperative fractures and the results are subject to reporting bias such that fractures not evident to the surgeon or not reported by the surgeon may be missed. The latter may have the effect of increasing the severity of fractures in the IOPFF group if there was a tendency to only report the worst fractures and increasing the likelihood that a fracture was included in the control group. We have used matching with regression but we are unable to determine the cause of death and as a result we are unable to directly ascribe the increased risk of death to the IOPFF or subsequent revision, even though the link between revision surgery and excess mortality has previously been established¹⁵. We are unable to review radiographs to establish fracture patterns, and treatment modalities. We assumed that the treatments given to hips in this study represented normal practice but we could not control for the effect of surgeon treatment choice on outcomes following IOPFF. These data do however represent “average” results for the “average” surgeon. Propensity score matching achieved excellent balance between groups but may not have controlled for unobserved characteristics which were important for both stem and patient survival. We were unable to adjust for all the relevant factors which determine post-operative mortality and implant failure since our data did not include radiographic or detailed co-morbidity information and as a result we are likely to be subject to errors due to confounding factors. In addition a small proportion of patients will experience implant failure without undergoing revision surgery (for example, conservative treatment or fixation of periprosthetic fracture) and as such will not be recorded in the NJR. Our approach might be improved with data linkage to hospital and primary care records. It is likely that linkage to patient reported outcome measures would further illuminate the true effect of IOPFF on patient outcomes.

Conclusions

We have demonstrated that IOPFF is associated with an increased risk of stem revision, revision for ASL, PFF, instability and patient mortality following primary THA. The risk of revision was dependent on IOPFF subtype, and the effect of IOPFF subtype is unique to each mode of failure. We have also demonstrated that patients with IOPFF have a higher risk of mortality than those without IOPFF, and this effect appears to be comprised of both an independent risk of IOPFF to the patient and the subsequent risk of revision surgery. Whilst the absolute risk of death is still low, it is clear that surgeons should make every effort to reduce the risk of IOPFF during primary THA through careful selection of implants and methods. Vigilant identification and treatment of IOPFF is recommended to prevent implant failure and reduce associated excess patient mortality. Further work to improve

methods of IOPFF identification on plain radiographs is required. When IOPFF does occur patients should be counselled regarding the increased risk of implant failure, revision operations and mortality.

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Table 1. Non-matched and matched cohort comparison

	Unmatched		SMD	Matched		SMD
<i>Group:</i>	No IOPFF	IOPFF		No IOPFF	IOPFF	
<i>n</i>	776409	4833		48154	4831	
<i>IOPFF subtype:</i>						
None (%)	776409 (100.0)			48154 (100.0)		
Calcar crack (%)		3018 (62.4)			3017 (62.5)	
Shaft fracture (%)		340 (7.0)			340 (7.0)	
Trochanteric fracture (%)		1475 (30.5)			1474 (30.5)	
<i>Patient Gender:</i>						
Female (%)	475029 (61.2)	3560 (73.7)	0.269*	35552 (73.8)	3558 (73.6)	0.004
<i>Mean age: years (range):</i>	69.25 (11 - 117)	68.26 (12 - 105)	0.083	68.27 (12 - 102)	68.25 (15 - 98)	0.001
<i>Age group:</i>			0.161*			0.083
11 <50 (%)	38225 (4.9)	390 (8.1)		3282 (6.8)	390 (8.1)	
50 <60 (%)	95318 (12.3)	672 (13.9)		6570 (13.6)	672 (13.9)	
60 <70 (%)	231378 (29.8)	1324 (27.4)		14300 (29.7)	1324 (27.4)	
70 <80 (%)	279469 (36.0)	1543 (31.9)		15997 (33.2)	1543 (31.9)	
80 <117 (%)	132019 (17.0)	904 (18.7)		8005 (16.6)	902 (18.7)	
<i>Side:</i>						
Right (%)	426349 (54.9)	2564 (53.1)	0.037	25716 (53.4)	2563 (53.1)	0.007
<i>ASA grade:</i>			0.158*			0.017
1 - Fit and healthy (%)	117874 (15.2)	729 (15.1)		7086 (14.7)	729 (15.1)	
2 - Mild disease not incapacitating (%)	534690 (68.9)	3046 (63.0)		30718 (63.8)	3046 (63.1)	
3 - Incapacitating systemic disease (%)	119598 (15.4)	1007 (20.8)		9842 (20.4)	1005 (20.8)	
4 - Life threatening disease (%)	4129 (0.5)	49 (1.0)		482 (1.0)	49 (1.0)	
5 - Expected to die within 24hrs (%)	118 (0.0)	2 (0.0)		26 (0.1)	2 (0.0)	
<i>Indication for surgery:</i>			0.276*			0.022
Acute trauma including hip fracture (%)	21685 (2.8)	146 (3.0)		1426 (3.0)	146 (3.0)	
Avascular necrosis (%)	10293 (1.3)	123 (2.5)		1180 (2.5)	123 (2.5)	
Previous trauma (%)	6974 (0.9)	168 (3.5)		1535 (3.2)	166 (3.4)	
Inflammatory arthritis (%)	8394 (1.1)	99 (2.0)		993 (2.1)	99 (2.0)	
Malignancy (%)	312 (0.0)	3 (0.1)		27 (0.1)	3 (0.1)	
Osteoarthritis (%)	717258 (92.4)	4103 (84.9)		41082 (85.3)	4103 (84.9)	
Other (%)	5651 (0.7)	68 (1.4)		660 (1.4)	68 (1.4)	
Paediatric disease (%)	5185 (0.7)	108 (2.2)		1132 (2.4)	108 (2.2)	
Previous arthrodesis (%)	236 (0.0)	2 (0.0)		17 (0.0)	2 (0.0)	
Previous infection (%)	421 (0.1)	13 (0.3)		102 (0.2)	13 (0.3)	

Table 1 continued	Unmatched		SMD	Matched		SMD
Approach:			0.055			0.005
Posterior (%)	447506 (57.6)	2669 (55.2)		26541 (55.1)	2669 (55.2)	
Anterolateral (%)	292455 (37.7)	1923 (39.8)		19218 (39.9)	1921 (39.8)	
Trochanteric osteotomy (%)	2986 (0.4)	13 (0.3)		121 (0.3)	13 (0.3)	
Other (%)	33462 (4.3)	228 (4.7)		2274 (4.7)	228 (4.7)	
Lead surgeon grade:						
Non consultant (%)	134866 (17.4)	847 (17.5)	0.004	8582 (17.8)	847 (17.5)	0.008
Organisation Type:			0.204*			0.009
National health service (%)	529370 (68.2)	3726 (77.1)		36959 (76.8)	3724 (77.1)	
Independent Hospital (%)	214471 (27.6)	984 (20.4)		9975 (20.7)	984 (20.4)	
Treatment centre (%)	32568 (4.2)	123 (2.5)		1220 (2.5)	123 (2.5)	
Stem fixation:						
Cementless (%)	338158 (43.6)	2969 (61.4)	0.364*	29524 (61.3)	2967 (61.4)	0.002
Surgical technique:						
Minimally invasive surgery (%)	53589 (6.9)	336 (7.0)	0.002	3340 (6.9)	336 (7.0)	0.001
Computer guided surgery (%)	20965 (2.7)	77 (1.6)	0.076	788 (1.6)	77 (1.6)	0.003
Thromboprophylaxis:						
Aspirin (%)	93989 (12.1)	443 (9.2)	0.095	5187 (10.8)	443 (9.2)	0.053
LMWH (%)	542559 (69.9)	3414 (70.6)	0.016	34048 (70.7)	3414 (70.7)	0.001
Pentasaccharide (%)	8785 (1.1)	62 (1.3)	0.014	512 (1.1)	62 (1.3)	0.02
Warfarin (%)	9539 (1.2)	67 (1.4)	0.014	606 (1.3)	67 (1.4)	0.011
Direct ThrombinInhibitor (%)	57713 (7.4)	415 (8.6)	0.042	3510 (7.3)	415 (8.6)	0.048
Factor Xa Inhibitor (%)	36140 (4.7)	203 (4.2)	0.022	2118 (4.4)	203 (4.2)	0.01
Other chemical prophylaxis (%)	53797 (6.9)	367 (7.6)	0.026	3569 (7.4)	365 (7.6)	0.005
Footpump (%)	204865 (26.4)	1212 (25.1)	0.03	12155 (25.2)	1212 (25.1)	0.004
TED (%)	506125 (65.2)	3142 (65.0)	0.004	31412 (65.2)	3141 (65.0)	0.005
Calf compression stocking (%)	304285 (39.2)	1987 (41.1)	0.039	19215 (39.9)	1986 (41.1)	0.025

Note: All results are sum total in group with percentage of variable total in parentheses apart from age which is also given as a mean with range. SMD = If SMD is <10% acceptable balance achieved. * = SMD >0.1. Stanadised mean difference, ASA = American Society of Anesthesiologists grade (pre-operative), LMWH = Low molecular weight Heparin,

