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Risk factors for intraoperative periprosthetic femoral fractures during primary total hip arthroplasty. An analysis from the National Joint Registry for England, Wales and the Isle of Man.

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1 **Risk factors for intraoperative periprosthetic femoral fractures during primary total hip**
2 **arthroplasty. An analysis from the National Joint Registry for England and Wales.**

3 **Abstract:**

4 *Background*

5 The aim of this study was to estimate risk factors for intraoperative periprosthetic femoral fractures
6 (IOPFF) and each anatomical subtype (calcar crack, trochanteric fracture, femoral shaft fracture)
7 during primary total hip arthroplasty (THA).

8 *Methods*

9 This retrospective cohort study included 793823 primary THAs between 2004 and 2016.
10 Multivariable regression modelling was used to estimate relative risk of patient, surgical and implant
11 factors for any IOPFF and for all anatomical subtypes of IOPFF. Clinically important interactions
12 were assessed using multivariable regression.

13 *Results*

14 Patient factors significantly increasing the risk of fracture were: female gender, American Association
15 of Anaesthesiologists (ASA) grade 3 to 5, pre-operative diagnosis including: avascular necrosis of the
16 hip (AVN), previous trauma, inflammatory disease, paediatric disease and previous infection. Overall
17 risk of IOPFF associated with age was greatest in patients below 50 years and above 80 years. Risk of
18 any fracture reduced with computer guided surgery (CGS) and in non-NHS hospitals. Non-posterior
19 approach's increased the risk of shaft and trochanteric fracture only. Cementless implants only
20 significantly increased the risk of calcar cracks and shaft fractures and not trochanteric fractures.

21 *Conclusions*

22 Fracture risk increases in patients less than 50 and older than 80, females, ASA grade 3 to 5 and
23 indications other than primary osteoarthritis. Large cumulative reduction in IOPFF risk may occur
24 with use of cemented implants, posterior approach and CGS.

25 Level of evidence: Level 3b (cohort study).

26 Key words: Total hip arthroplasty; complications; intraoperative periprosthetic fracture; risk
27 factors

28 **Background:**

29 Total hip arthroplasty (THA) is a highly successful procedure with a low complication rate. Further
30 improvements in outcomes rely on incremental reduction of complications associated with poorer
31 outcomes. One significant complication is intraoperative periprosthetic femoral fracture (IOPFF).
32 IOPFF can occur in the trochanteric region, calcar or femoral diaphysis[1]. Incidence of IOPFF in
33 primary THA ranges from 1–5%[2-4]. Most IOPFF occur during canal preparation and stem
34 implantation [2], when the circumferential strains of the proximal femur are highest[5]. Large strains
35 can occur when the surgeon establishes implant stability through press-fit fixation with cementless
36 femoral implants[6], which increases the risk of IOPFF with cementless femoral implants[2, 3, 7].
37 IOPFF has been linked to an increased risk of post-operative periprosthetic fracture (PFF) and
38 increased revision risk[2, 8, 9]. Reduced implant survival in cementless implants is perhaps due to
39 failure of primary stability even following adequately treated IOPFF[9].

40 Prevention of IOPFF by adjusting methods to suit the risk profile of the patient is an obvious means to
41 reduce patient harm and further improve stem survival. Non modifiable risk factors include female
42 sex, increasing age, poor bone quality, abnormal proximal femur morphology[2, 4, 7, 8, 10].

43 Established modifiable risk factors include cementless stem fixation and surgical approach (direct
44 anterior and Hardinge)[9, 11, 12]. IOPFF is relatively uncommon and previous studies have lacked
45 the size and power to accurately identify other relevant predictors such as computer guided surgery
46 (CGS) or provider organisation type. Current evidence has failed to estimate risk factors for all
47 subtypes of IOPFF. A deeper understanding of how risk factors relate to the specific anatomical
48 subtype of IOPFF will help to develop an understanding of the mechanism by which the increased
49 risk occurs and thus how it can be reduced by future development of approaches, surgical techniques
50 and implants.

51 The aim was to identify the predictors for all IOPFF, and for each anatomical subtype in the National
52 Joint Registry (NJR) for England and Wales, the largest joint registry in the world.

53

54 **Materials and Methods:**

55 *Database*

56 The NJR has recorded all THAs performed at hospitals in England and Wales since 2003. Patient data
57 and surgical data are collected for each hip arthroplasty. Surgeon-reported IOPFF, have been
58 collected since 1st April 2004. This study included all primary THAs using stemmed implants in the
59 NJR from 1st April 2004 to 30th September 2016.

60

61 *Participants*

62 793 977 THAs were eligible for analysis. Exclusions were; cases from the Isle of Man (low numbers,
63 n= 153). The resulting subset of data included 793 823 primary THA. Institutional ethical approval
64 was granted and the manuscript was approved by the NJR.

65

66 *Variables*

67 All variables relating to patient age (years), gender, ASA group (1-2 versus 3-5), year of surgery, side
68 of operation, surgical approach (anterolateral [Hardinge, anterolateral and lateral], trochanteric
69 osteotomy, posterior, other), computer guided surgery (CGS), minimally invasive surgery, surgeon
70 grade (consultant versus non-consultant), hospital type (National Health Service [NHS], Independent
71 hospital, Independent treatment centre), indication (osteoarthritis [OA], trauma including fractured
72 neck of femur [NOF], avascular necrosis [AVN], inflammatory arthritis, previous trauma, paediatric
73 hip disease [congenital dysplasia of the hip, Perthes, skeletal dysplasia, slipped upper femoral
74 epiphysis], malignancy, previous arthrodesis, previous infection and other) and stem fixation type
75 (cemented versus cementless) were included. Year of implantation was used to estimate change in
76 incidence of IOPFF with each subsequent year in the registry dataset (cohort effect).

77

78 *Outcome*

79 The study outcome was the occurrence of an IOPFF. Reported untoward intraoperative events in the
80 NJR include: “calcar crack”, “shaft fracture”, “shaft penetration”, “trochanteric fracture” and “other”.
81 We included IOPFF as either “calcar crack”, “shaft fracture”, “shaft penetration”, “trochanteric
82 fracture” and text describing IOPFF in “other”. Cases were grouped as calcar, trochanter or shaft
83 fractures (shaft fracture and penetration). Shaft penetration was subsequently dropped because none
84 were recorded.

85

86 *Statistical analysis:*

87 Analysis was conducted in two parts: firstly, prevalence and risk factors for any IOPFF and secondly
88 prevalence and risk factors for each IOPFF subtype. Univariate comparisons of continuous variables
89 were performed with unpaired t-tests, and comparisons of categorical variables were performed with
90 chi-square tests. Multiple comparison of continuous variables were performed with Pearson χ^2 tests.
91 Since the dataset was large and multiple comparisons were made, a significance level of $p < 0.01$ was
92 chosen. A binary multivariable logistic regression model estimated the relative risk (RR) of IOPFF
93 and 95% confidence interval (CI) for each variable compared to normal practice where applicable.
94 The model includes all variables and estimates the individual effect of each variable whilst adjusting
95 for the effects of others and confidence intervals are given to reflect uncertainty of these estimates. In
96 the second part of the analysis, modelling was repeated for fractures of the calcar, shaft and trochanter
97 separately. All analyses were performed using R (v3.5.1, R, Vienna, Austria[13]). Models were
98 assessed using the concordance statistic (C-statistic). Age was determined to be non-linear through
99 fitting of higher order terms, for clarity age was categorised into five groups (<50, 50<60, 60<70,
100 70<80, 80+ years). Interactions were selected a priori by authors JL and HP and tested by the addition
101 of a single interaction term to the original multivariable models for all IOPFF and each anatomical
102 subtype in turn (Appendix 1). The addition of interaction terms was performed in a single step and
103 repeated for each term. Age was included as a continuous variable to increase accuracy of modelling.
104 The interaction term results of interaction terms on the multivariable models were assessed visually if
105 the interaction term reached statistical significance ($p < 0.01$, table 5).

106 To estimate the overall relative effect of changing all significant modifiable risk factors, comparisons
107 were modelled to calculate the RR (95% CI) of best versus worst practice. The average risk ratio of
108 IOPFF was calculated comparing typical OA hip patients (female, between 60 and 70 years, ASA 1 or
109 2) undergoing THA with the worst and best selection of modifiable risk factors.

110

111

112 **Results:**

113 *Part one: All IOPFF*

114 The prevalence of IOPFF during primary THA was 0.62% (4938/793 823). The prevalence of IOPFF
115 more than doubled in patients with cementless compared with cemented femoral implants (0.87%
116 versus 0.42%) (p<0.001). Mean age (SD) of patients in the IOPFF group was statistically different to
117 those without IOPFF (68.3 (12.7) years versus 69.2 (11.0) years) (p<0.001) although not clinically
118 relevant. IOPFF occurred more commonly in younger (<50) and older (>80) patients. There were a
119 greater proportion of female patients with IOPFF than those without (73.7% versus 61.2%) (p<0.001).
120 A greater proportion of patients with IOPFF had a non-OA diagnosis (p<0.001) (table 1).

121 *Risk factors for IOPFF*

122 Relative risk of IOPFF almost doubled in females (RR 1.91 (CI 1.79-2.03) (Table 2). Risk of IOPFF
123 increased significantly in the young (age <50, RR 1.21 [CI 1.08-1.37]) and older patients (>80, RR
124 1.23 [CI 1.14-1.34]) versus patients between 70 and 80 years (p<0.01). Risk of IOPFF was 1.08 in left
125 sided THA (CI 1.02-1.14) (p<0.01). Risk of IOPFF increased with worse ASA group (3-5) (RR 1.45
126 [CI 1.35-1.55]). All non-OA indications significantly increased the risk of IOPFF apart from acute
127 trauma and malignancy. Surgical predictors increasing the risk of IOPFF included cementless femoral
128 implants (RR 2.40 [CI 2.26-2.55]) and anterolateral approach (RR 1.09 [CI 1.03-1.16]). Risk of
129 IOPFF was significantly reduced when THA was performed in a non-NHS hospital or when CGS was
130 used (RR 0.51 [CI 0.41-0.65]) (p<0.01).

131

132 *Part two: IOPFF subtypes*

133 Fractures affecting the calcar were most common (n = 3080) (table 3). Calcar cracks occurred more
134 frequently in patients <60 when compared to other fracture types. A smaller proportion of patients
135 with shaft fractures were female when compared to calcar and trochanteric fractures (69.9% versus
136 72.7% and 77.0%) (p=0.002). Cementless implants were used more commonly in calcar fractures than
137 shaft or trochanteric fractures (73.0% versus 53.7% and 39.8% respectively) (p<0.001).

138

139 *Risk factors for IOPFF by fracture subtype*

140 Patient factors increasing the risk of IOPFF in each fracture subtype were female gender and ASA
141 grade 3 to 5 (Table 4). Relationship between age and risk of IOPFF varied by fracture subtype (figure
142 2). Risk of calcar crack significantly increased in the youngest age groups (50<60 [RR 1.18 (1.05-
143 1.31)], <50 [RR 1.52 (CI 1.33-1.75)] p<0.01). Risk of shaft fracture increased significantly in patients
144 over 80 (RR 1.93 [CI 1.47-2.54] p<0.01). Risk of trochanteric fracture increased steadily with age.
145 Indications for THA which increase IOPFF risk for all fracture locations included previous trauma
146 and paediatric disease. Risk of calcar crack also increased for surgical indications including AVN,
147 inflammatory disease, previous infection and “other”. Risk of shaft fracture increased for surgical
148 indications including previous infection and “other”. Risk of trochanteric fracture increased for
149 surgical indication of AVN and inflammatory hip disease.

150 Cementless implants more than doubled the risk of calcar (RR 3.76 [CI 3.46 – 4.09], p<0.01) and
151 shaft fracture subtypes (RR 2.05 [CI 1.64-2.56], p<0.01). Posterior approach and CGS significantly
152 decreased the risk of shaft fractures and trochanteric fractures.

153

154 *Interactions between risk factors*

155 The predicted prevalence of any IOPFF increased with cementless stems and worsening ASA group
156 but the prevalence was highest when cementless stems were used (fig 1A). The predicted prevalence
157 of IOPFF on patients with cementless stems was not age dependent and was greater than the
158 prevalence predicted when using a cemented stem although the risk of IOPFF increased with age (fig.
159 1B). Predicted prevalence of any IOPFF increased with age in patients with OA, whereas patients
160 with a diagnosis of ‘acute trauma including NOF’ and ‘other’ were predicted to experience an inverse
161 relationship, with higher prevalence of any IOPFF in younger age groups (fig. 1C). The relationship
162 between age and diagnosis remained consistent to the overall effect when patients underwent surgery
163 for OA (fig. 1D, left). Patients with a diagnosis of ‘other’ were predicted higher prevalence of any
164 IOPFF when using cemented and cementless stems in younger age groups and the prevalence of any

165 IOPPF decreased in older patients (fig. 1D, right). The predicted prevalence of calcar crack increased
166 in females versus males and in cementless versus cemented stem but the effect of cementless stems on
167 risk of calcar crack was much larger for females than males (fig. 1E). The predicted prevalence of
168 calcar cracks increased in younger patients in those undergoing THA with cementless stems, whereas
169 the predicted prevalence of calcar cracks with cemented stems was consistently low across the age
170 range of patients in the study (fig. 1F). The predicted prevalence of shaft fracture was much increased
171 in older females, whereas the predicted prevalence of shaft fracture remained consistently low across
172 all ages with cemented implants (fig. 1G). The predicted prevalence of trochanteric fracture was
173 higher in younger patients when THA was performed for acute trauma including NOF in comparison
174 to THA performed for osteoarthritis (fig. 1H). Predicted prevalence of trochanteric fracture was
175 highest in consultants performing ‘other’ approaches compared to non-consultants using the same
176 approach, whereas predicted prevalence of trochanteric fracture was roughly equivalent between lead
177 surgeon grades using other approaches (fig. 1I). The fixed effects of statistically significant
178 interactions are given in table 5.

179 *Effects of combined predictors*

180 Combined relative risk of shaft IOPPF was 7.49 (CI 2.78 - 20.02) when using the worst (cementless
181 stem via “other” or Anterolateral approach without CGS) versus the best (cemented stem via posterior
182 approach with CGS) selection of modifiable risk factors when operating on a typical OA hip patient
183 (table 5) ($p < 0.01$).

184 **Discussion:**

185 This paper is the largest study reporting risk factors for IOPFF subtypes during primary THA. It
186 outlines new risk factors for IOPFF which can be used to identify and protect patients undergoing
187 THA. Risk of IOPFF is highest at extremes of age and not just the older patient population. Higher
188 preoperative ASA grade is associated with increased risk of IOPFF. IOPFF risk did not rise in hip
189 fracture but did increase in all other non-OA diagnoses. Cementless stem use is associated with
190 increased risk of calcar and shaft fractures. Cementless stems appear to be an age independent risk
191 factor for any IOPFF. Anterolateral and ‘other’ approaches can increase the risk of trochanteric and
192 shaft fractures versus posterior approach. Computer guided surgery reduced risk of any IOPFF and its
193 effect appeared to affect all patients consistently. With judicious adjustment of modifiable risk factors,
194 a potential seven-fold reduction in relative risk of IOPFF may be achieved.

195 *Patient related risk factors for IOPFF*

196 The risk of IOPFF approximately doubles in females[2, 4, 8, 14]. These results have shown an
197 increasing predicted prevalence of shaft fracture with increasing age in females, but no other
198 interaction effect of age on gender in other anatomical subtypes. Gender differences and gender-age
199 interactions may exist because females are affected by post-menopausal osteoporosis which reduces
200 bone strength[15]. The greatest age associated risk was seen in both patients below 50 years and
201 above 80 years old. Prevalence of any IOPFF increased in younger patients with acute fracture and
202 ‘other’ indications relative to patients with OA. Increasing age has been previously associated with
203 higher IOPFF fracture risk[2, 4]. Young patients may be at greater risk of calcar and shaft fractures
204 because the proximal femoral canal is typically tighter and requires more prolonged and forceful
205 rasping. Many young patients requiring hip replacement have dysplastic proximal femora which may
206 be particularly narrow or osteoporotic. The risk of trochanteric fracture increased with age in patients
207 with OA but analysis of interactions demonstrated that the predicted prevalence of trochanteric
208 fracture decreased with age to below that of OA in older patients with a diagnosis of acute fracture
209 including NOF. Given that the metaphyseal bone of the trochanter is particularly vulnerable to
210 osteoporosis, it is not clear why this might be observed. Perhaps increased surgeon awareness of
211 osteoporosis in patients with NOF may reduce the risk of trochanteric injury.

212 Patients undergoing left sided THA have an 8% increased risk of IOPFF ($p<0.001$) (table 2). This
213 could be due to surgeon handedness, which has been shown to affect surgical performance during
214 THA[16].

215 Inflammatory arthritis, previous trauma and NOF are commonly associated with periarticular
216 osteoporosis and increased risk of IOPFF. This study did not find increased risk of IOPFF with THA
217 for NOF, which is a surprising finding. Patients with NOF are typically older and perhaps more likely
218 to have a wider proximal femoral canal, which reduces femoral stem mismatch. This study confirmed

219 that AVN, previous trauma and previous infection were associated with a significant increase in
220 IOPFF risk[4]. Exposure to steroids, associated osteopenia and / or post-operative bone loss or
221 fibrosis may make exposure and femoral canal preparation precarious. Worse ASA grade is strongly
222 associated with increased IOPFF risk. ASA is likely to be a surrogate marker for health conditions
223 which can affect the integrity of the proximal femoral bone stock. ASA grade may be a useful
224 discriminator for surgeons deciding which implants and techniques to adopt.

225

226 *Surgery / surgeon related risk factors for IOPFF*

227 Increased relative risk of IOPFF associated with cementless implant usage is reflected universally in
228 the literature [2, 3, 8-10, 17, 18]. We have demonstrated that the effect of cementless stem use
229 resulted in a constant elevated predicted prevalence of any IOPFF across all age ranges. Associated
230 risk of calcar and shaft fractures also independently increased with cementless stem use. Calcar or
231 shaft fractures tend to occur during canal preparation and stem insertion[2] where most cementless
232 femoral implants use a press fit which increases femoral cortical strains[6]. The increased risk of
233 calcar crack associated with cementless stems was most noticeable in female patients and there was
234 no significant age-gender interaction when predicting calcar cracks. It is possible that there are gender
235 differences between the morphology of female and male proximal femurs which may predispose
236 female to calcar cracks during cementless stem implantation but there is little evidence to support this
237 observation.

238 Cementless stem survival has previously been shown to be better in a younger population of patients
239 perhaps because of better bone stock which reduces the risk of perioperative complications like
240 IOPFF and PFF[19]. In younger patients where it has been shown that cementless femoral stems may
241 survive longer the increased risk of IOPFF and associated sequelae must be weighed up against the
242 potential benefit in stem survival, particularly in patients with proximal femoral features appear weak
243 or which may require prolonged or forceful preparation. The decision to use cementless or a
244 cemented stem is complex and given that risk of IOPFF increased in the youngest patients in this
245 study perhaps surgeons and policy makers should use other standardised variables to identify groups
246 in which survival with cementless stems is better.

247 Surgical approach to the hip is a contentious topic with rising popularity of the direct anterior
248 approach because of potentially reduced dislocation rates and faster recovery. Hardinge approach has
249 previously been identified as a risk factor for IOPFF[8, 9, 11, 17]. The Hardinge and direct anterior
250 approach can place significant forces on trochanteric muscle attachments and the femur, which are
251 under tension during canal preparation and implantation[11, 12]. Increased rotational loading of the
252 trochanter and shaft during anterolateral and other approaches may explain the specific increased risk
253 of IOPFF. These results predicted that consultant surgeons experienced a higher prevalence of

254 trochanteric fractures during ‘other’ approaches compared to non-consultant grade surgeons. This is
255 likely to be the result of selection bias, with consultant surgeons electing to perform ‘other’
256 approaches on more challenging cases. The absolute predicted risk of consultant lead surgeons
257 performing ‘other’ approaches was higher than any other group and highlights the particular risk
258 associated with these approaches. Further work to adapt these approaches to reduce femoral strains
259 may help to reduce associated risk of IOPFF.

260 This is the first study to demonstrate an association between CGS and a reduced risk of any IOPFF,
261 calcar and trochanteric subtypes. CGS typically requires pre-operative 3D imaging, which may allow
262 more accurate planning of implant size and can give feedback on direction of femoral preparation and
263 implantation. There were no clinically plausible interactions between CGS and other variables in this
264 study. This may suggest that CGS is an independent protective factor against any IOPFF. However,
265 confounding may exist since CGS may also be a surrogate marker for careful higher volume surgeons
266 and surgeons may select easier or more difficult cases for CGS assistance. We identified higher
267 incidence of IOPFF in patients undergoing surgery in public hospitals. In the UK surgery undertaken
268 in independent hospital are more likely to be performed by consultant surgeons and patients tend to be
269 fitter and cases less complex which may introduce confounding. Although the overall risk of IOPFF
270 seems low, the surgeon is able to reduce the risk significantly further by modifying all possible risk
271 factors which they have control over.

272 This observational study benefits from the power of large numbers which can give insight into
273 relatively rare complications but are constrained by the innate availability of data. There are important
274 risk factors which cannot be included such as proximal femoral morphology, proximal femoral bone
275 mineral density, specific implant/rasp design and shape, force of impaction and control over surgical
276 techniques. Given this constraint, the performance of models used in this study are adequate but
277 results should be appraised alongside other data. NJR IOPFF data are self-reported immediately after
278 surgery and may miss shaft fractures which are only seen on post-operative radiographs. This may
279 explain why there are no reported shaft penetrations in this study. Abdel *et al*[2] reported 5.6% of all
280 IOPFF were shaft fractures and 24% of these were discovered on post-operative radiographs. In this
281 study shaft IOPFF accounted for 7.1 % of all IOPFF, but this may be an underestimate given these
282 limitations. Cementless femoral implants may be used preferentially in cases of IOPFF if the surgeon
283 prefers to use a cementless distally fixing modular implant, which may bias results. However,
284 cementless modular implants were used in only 3.2% of all the IOPFF in our analysis, which could
285 introduce only a small error into our estimates of the effect of fixation. Not all variables identified in
286 multivariable regression were selected using the ctree analysis. This is likely to be because ctree
287 analysis was performed on a smaller and smaller subgroup reducing the likelihood of a relatively
288 infrequently occurring variable being selected by the algorithm. The analysis of stem properties
289 associated with intraoperative fracture is not feasible as the NJR only records the final implant used

290 and not the precise preparation equipment (rasps and or reamers) used. It is likely that the numbers
291 reported here are an underestimate of IOPFF as the fractures are only reported if the surgeon is aware
292 of their occurrence during surgery.

293 *Conclusions*

294 The risk of all IOPFF increases in females, less fit patients and in those with a non-OA indication for
295 surgery. Large cumulative reduction in IOPFF risk appears associated with use of cemented implants,
296 posterior approach and CGS. Understanding the effect of combined factors is paramount when
297 choosing the safest technique and implant choice to minimise IOPFF and future revision risk. Future
298 work should elucidate the effect of CGS as well as direct anterior approach on the risk of IOPFF
299 given that there are significant effects of CGS and the use of direct anterior approach is increasing.
300 Although there is some evidence to suggest a link between IOPFF and poorer implant survival, further
301 analysis to assess the impact of IOPFF subtypes on patient and implant survival is required.

302

303

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Table 1. Summary descriptive statistics for primary total hip arthroplasty with and without IOPFF during primary surgery

	No IOPFF	IOPFF	p overall
<i>Side</i>			0.010
Left	355794 (45.10%)	2318 (46.94%)	
Right	433091 (54.90%)	2620 (53.06%)	
<i>Gender</i>			<0.001*
Female	482627 (61.18%)	3644 (73.80%)	
Male	306258 (38.82%)	1294 (26.20%)	
<i>Age group</i>			<0.001*
11 to 49	39044 (4.95%)	401 (8.12%)	
50 to 59	97113 (12.31%)	693 (14.03%)	
60 to 69	235370 (29.84%)	1346 (27.26%)	
70 to 79	283522 (35.94%)	1567 (31.73%)	
80 to 117	133836 (16.97%)	931 (18.85%)	
<i>ASA group</i>			<0.001*
1 and 2	663279 (84.08%)	3857 (78.11%)	
3 to 5	125606 (15.92%)	1081 (21.89%)	
<i>Indication</i>			<0.001*
Osteoarthritis	728589 (92.36%)	4194 (84.93%)	
Acute trauma including hip fracture	22003 (2.79%)	148 (3.00%)	
Avascular necrosis	10476 (1.33%)	123 (2.49%)	
Previous trauma	7116 (0.90%)	174 (3.52%)	
Inflammatory arthritis	8559 (1.08%)	102 (2.07%)	
Malignancy	324 (0.04%)	3 (0.06%)	
Other	5841 (0.74%)	68 (1.38%)	
Paediatric disease	5301 (0.67%)	111 (2.25%)	
Previous arthrodesis	242 (0.03%)	2 (0.04%)	
Previous infection	434 (0.06%)	13 (0.26%)	
<i>Stem fixation</i>			<0.001*
Cemented	444464 (56.34%)	1901 (38.50%)	
Cementless	344421 (43.66%)	3037 (61.50%)	
<i>Lead surgeon grade</i>			0.895
Consultant	651974 (82.64%)	4077 (82.56%)	
Non consultant	136911 (17.36%)	861 (17.44%)	
<i>Organisation type</i>			<0.001*
NHS	538645 (68.28%)	3813 (77.22%)	
Independent hospital	217267 (27.54%)	999 (20.23%)	
Treatment centre	32973 (4.18%)	126 (2.55%)	
<i>Approach</i>			0.002*
Posterior	454410 (57.60%)	2721 (55.10%)	
Anterolateral	297413 (37.70%)	1967 (39.83%)	
Trochanteric Osteotomy	3017 (0.38%)	14 (0.28%)	
Other	34045 (4.32%)	236 (4.78%)	
<i>Surgical technique</i>			1.000
Minimally invasive surgery			
No	734071 (93.05%)	4595 (93.05%)	
Yes	54814 (6.95%)	343 (6.95%)	
Computer guided surgery			<0.001*
No	767299 (97.26%)	4857 (98.36%)	
Yes	21586 (2.74%)	81 (1.64%)	

Note: Results are numbers (% of column within group). ASA denotes American society of Anaesthesiologists grade, NHS is National Health Service. *p<0.01.

Table 2. Results from multivariable regression demonstrating risk factors for any IOPFF during primary total hip arthroplasty

	Relative risk of IOPFF (95% confidence interval)
<i>Side</i>	
Left	1.08 (1.02 - 1.14)*
Right	1
<i>Gender</i>	
Female	1.91 (1.79 - 2.03)*
Male	1
<i>Age group</i>	
11 to 49	1.21 (1.08 - 1.37)*
50 to 59	1.05 (0.95 - 1.15)
60 to 69	0.94 (0.87 - 1.01)
70 to 79	1
80 to 117	1.23 (1.14 - 1.34)*
<i>ASA group</i>	
1 and 2	1
3 to 5	1.45 (1.35 - 1.55)*
<i>Indication</i>	
Osteoarthritis	1
Acute trauma including hip fracture	1.13 (0.96 - 1.34)
Avascular necrosis	1.81 (1.51 - 2.17)*
Previous trauma	3.80 (3.27 - 4.42)*
Inflammatory arthritis	1.75 (1.44 - 2.13)*
Malignancy	2.01 (0.65 - 6.22)
Other	1.85 (1.45 - 2.35)*
Paediatric disease	2.78 (2.28 - 3.38)*
Previous arthrodesis	1.25 (0.31 - 4.96)
Previous infection	4.92 (2.88 - 8.40)*
<i>Stem fixation</i>	
Cemented	1
Cementless	2.40 (2.26 - 2.55)*
<i>Lead surgeon grade</i>	
Consultant	1
Non consultant	0.96 (0.89 - 1.04)
<i>Organisation type</i>	
NHS	1
Independent hospital	0.68 (0.63 - 0.73)*
Treatment centre	0.58 (0.49 - 0.70)*
<i>Approach</i>	
Posterior	1
Anterolateral	1.09 (1.03 - 1.16)*
Trochanteric Osteotomy	0.97 (0.57 - 1.63)
Other	1.08 (0.94 - 1.23)
<i>Surgical technique</i>	
Minimally invasive surgery	0.98 (0.87 - 1.10)
Computer guided surgery	0.51 (0.41 - 0.65)*
<i>Cohort effect</i>	
Subsequent year of primary surgery	0.97 (0.96 - 0.97)*
Observations	793,823
C - statistic	0.68

Note: Results are relative risks (95% confidence intervals). ASA denotes American society of Anaesthesiologists grade, NHS is National Health Service. *Ins* denotes insufficient numbers for meaningful analysis. *p<0.01

Table 3. Summary descriptive statistics for primary total hip arthroplasty with and without IOPFF subtypes during primary surgery

	Calcar cracks n = 3080	Shaft fractures n = 352	Trochanteric fractures n = 1506	p overall
<i>Side</i>				0.980
Left	1444 (46.88%)	167 (47.44%)	707 (46.95%)	
Right	1636 (53.12%)	185 (52.56%)	799 (53.05%)	
<i>Gender</i>				0.002*
Female	842 (27.34%)	106 (30.11%)	346 (22.97%)	
Male	2238 (72.66%)	246 (69.89%)	1160 (77.03%)	
<i>Age group</i>				<0.001*
11 to 49	330 (10.71%)	28 (7.95%)	43 (2.86%)	
50 to 59	511 (16.59%)	30 (8.52%)	152 (10.09%)	
60 to 69	899 (29.19%)	82 (23.30%)	365 (24.24%)	
70 to 79	906 (29.42%)	106 (30.11%)	555 (36.85%)	
80 to 117	434 (14.09%)	106 (30.11%)	391 (25.96%)	
<i>ASA group</i>				<0.001*
1 and 2	2534 (82.27%)	251 (71.31%)	1072 (71.18%)	
3 to 5	546 (17.73%)	101 (28.69%)	434 (28.82%)	
<i>Indication</i>				0.001*
Osteoarthritis	2630 (85.39%)	280 (79.55%)	1284 (85.26%)	
Acute trauma including hip fracture	86 (2.79%)	11 (3.12%)	51 (3.39%)	
Avascular necrosis	84 (2.73%)	6 (1.70%)	33 (2.19%)	
Previous trauma	92 (2.99%)	30 (8.52%)	52 (3.45%)	
Inflammatory arthritis	54 (1.75%)	8 (2.27%)	40 (2.66%)	
Malignancy	1 (0.03%)	0 (0.00%)	2 (0.13%)	
Other	43 (1.40%)	7 (1.99%)	18 (1.20%)	
Paediatric disease	80 (2.60%)	8 (2.27%)	23 (1.53%)	
Previous arthrodesis	1 (0.03%)	0 (0.00%)	1 (0.07%)	
Previous infection	9 (0.29%)	2 (0.57%)	2 (0.13%)	
<i>Stem fixation</i>				<0.001*
Cemented	831 (26.98%)	163 (46.31%)	907 (60.23%)	
Cementless	2249 (73.02%)	189 (53.69%)	599 (39.77%)	
<i>Lead surgeon grade</i>				<0.001*
Consultant	2601 (84.45%)	294 (83.52%)	1182 (78.49%)	
Non consultant	479 (15.55%)	58 (16.48%)	324 (21.51%)	
<i>Organisation type</i>				<0.001*
NHS	2278 (73.96%)	262 (74.43%)	1273 (84.53%)	
Independent hospital	713 (23.15%)	80 (22.73%)	206 (13.68%)	
Treatment centre	89 (2.89%)	10 (2.84%)	27 (1.79%)	
<i>Approach</i>				<0.001*
Posterior	1839 (59.71%)	160 (45.45%)	722 (47.94%)	
Anterolateral	1109 (36.01%)	164 (46.59%)	694 (46.08%)	
Trochanteric Osteotomy	8 (0.26%)	2 (0.57%)	4 (0.27%)	
Other	124 (4.03%)	26 (7.39%)	86 (5.71%)	
<i>Surgical technique</i>				0.002*
Minimally invasive surgery				
Yes	244 (7.92%)	20 (5.68%)	79 (5.25%)	
No	2836 (92.08%)	332 (94.32%)	1427 (94.75%)	
Computer guided surgery				0.723
Yes	3026 (98.25%)	347 (98.58%)	1484 (98.54%)	
No	54 (1.75%)	5 (1.42%)	22 (1.46%)	

Note: Results are numbers (% of column within group). ASA denotes American society of Anaesthesiologists grade, NHS is National Health Service. *p<0.01.

Table 4. Results from multivariable regression demonstrating risk factors for IOPFF subtypes

	Relative risk (95% confidence interval)		
	Calcar cracks	Shaft fractures	Trochanteric fractures
<i>Side</i>			
Left	1.07 (1.00 - 1.15)	1.09 (0.88 - 1.34)	1.10 (0.99 - 1.22)
Right	1	1	1
<i>Gender</i>			
Female	1.91 (1.76 - 2.06)*	1.46 (1.16 - 1.84)*	2.06 (1.82 - 2.32)*
Male	1	1	1
<i>Age group</i>			
11 to 49	1.52 (1.33 - 1.75)*	1.30 (0.82 - 2.05)	0.46 (0.33 - 0.64)*
50 to 59	1.18 (1.05 - 1.31)*	0.71 (0.47 - 1.07)	0.83 (0.69 - 0.99)
60 to 69	1.00 (0.91 - 1.09)	0.88 (0.66 - 1.18)	0.84 (0.73 - 0.96)
70 to 79	1	1	1
80 to 117	1.09 (0.97 - 1.22)	1.93 (1.47 - 2.54)*	1.29 (1.13 - 1.47)*
<i>ASA group</i>			
1 and 2	1	1	1
3 to 5	1.27 (1.16 - 1.40)*	1.79 (1.40 - 2.29)*	1.69 (1.50 - 1.90)*
<i>Indication</i>			
Osteoarthritis	1	1	1
Acute trauma including hip fracture	1.25 (1.00 - 1.55)	1.26 (0.68 - 2.32)	0.95 (0.72 - 1.26)
Avascular necrosis	1.85 (1.48 - 2.31)*	1.35 (0.60 - 3.08)	1.89 (1.33 - 2.68)*
Previous trauma	3.63 (2.95 - 4.46)*	9.01 (6.14 - 13.24)*	3.09 (2.34 - 4.08)*
Inflammatory arthritis	1.47 (1.13 - 1.93)*	2.21 (1.09 - 4.50)	2.30 (1.68 - 3.16)*
Malignancy	1.42 (0.20 - 10.05)	<i>ins</i>	2.97 (0.74 - 11.90)
Other	1.87 (1.38 - 2.53)*	2.82 (1.32 - 6.00)*	1.61 (1.01 - 2.56)
Paediatric disease	2.58 (2.04 - 3.25)*	3.75 (1.76 - 7.95)*	3.58 (2.32 - 5.53)*
Previous arthrodesis	0.94 (0.13 - 6.62)	<i>ins</i>	2.24 (0.32 - 15.84)
Previous infection	5.27 (2.76 - 10.05)*	12.00 (2.97 - 48.58)*	2.87 (0.72 - 11.48)
<i>Stem fixation</i>			
Cemented	1	1	1
Cementless	3.76 (3.46 - 4.09)*	2.05 (1.64 - 2.56)*	1.13 (1.02 - 1.26)
<i>Lead surgeon grade</i>			
Consultant	1	1	1
Non consultant	0.96 (0.86 - 1.06)	0.89 (0.67 - 1.20)	0.98 (0.86 - 1.11)
<i>Organisation type</i>			
NHS	1	1	1
Independent hospital	0.77 (0.70 - 0.84)*	0.91 (0.70 - 1.19)	0.46 (0.40 - 0.54)*
Treatment centre	0.63 (0.51 - 0.79)*	0.82 (0.43 - 1.55)	0.41 (0.28 - 0.60)*
<i>Approach</i>			
Posterior	1	1	1
Anterolateral	0.94 (0.87 - 1.02)	1.54 (1.23 - 1.93)*	1.36 (1.22 - 1.51)*
Trochanteric Osteotomy	1.03 (0.51 - 2.05)	2.03 (0.51 - 8.16)	0.77 (0.29 - 2.05)
Other	0.83 (0.69 - 1.00)	2.06 (1.36 - 3.12)*	1.51 (1.21 - 1.89)*
<i>Surgical technique</i>			
Minimally invasive surgery	1.01 (0.88 - 1.16)	0.82 (0.50 - 1.32)	0.92 (0.72 - 1.18)
Computer guided surgery	0.53 (0.40 - 0.71)*	0.49 (0.19 - 1.25)	0.48 (0.31 - 0.76)*
<i>Cohort effect</i>			
Subsequent year of primary	0.96 (0.95 - 0.97)*	0.96 (0.93 - 0.99)	0.98 (0.97 - 1.00)
Observations	791,965	788,671	790,391
C - statistic	0.71	0.69	0.68

Note: Results are relative risks (95% confidence intervals). ASA denotes American society of Anaesthesiologists grade, NHS is National Health Service. *Ins* denotes insufficient numbers for meaningful analysis. *p<0.01

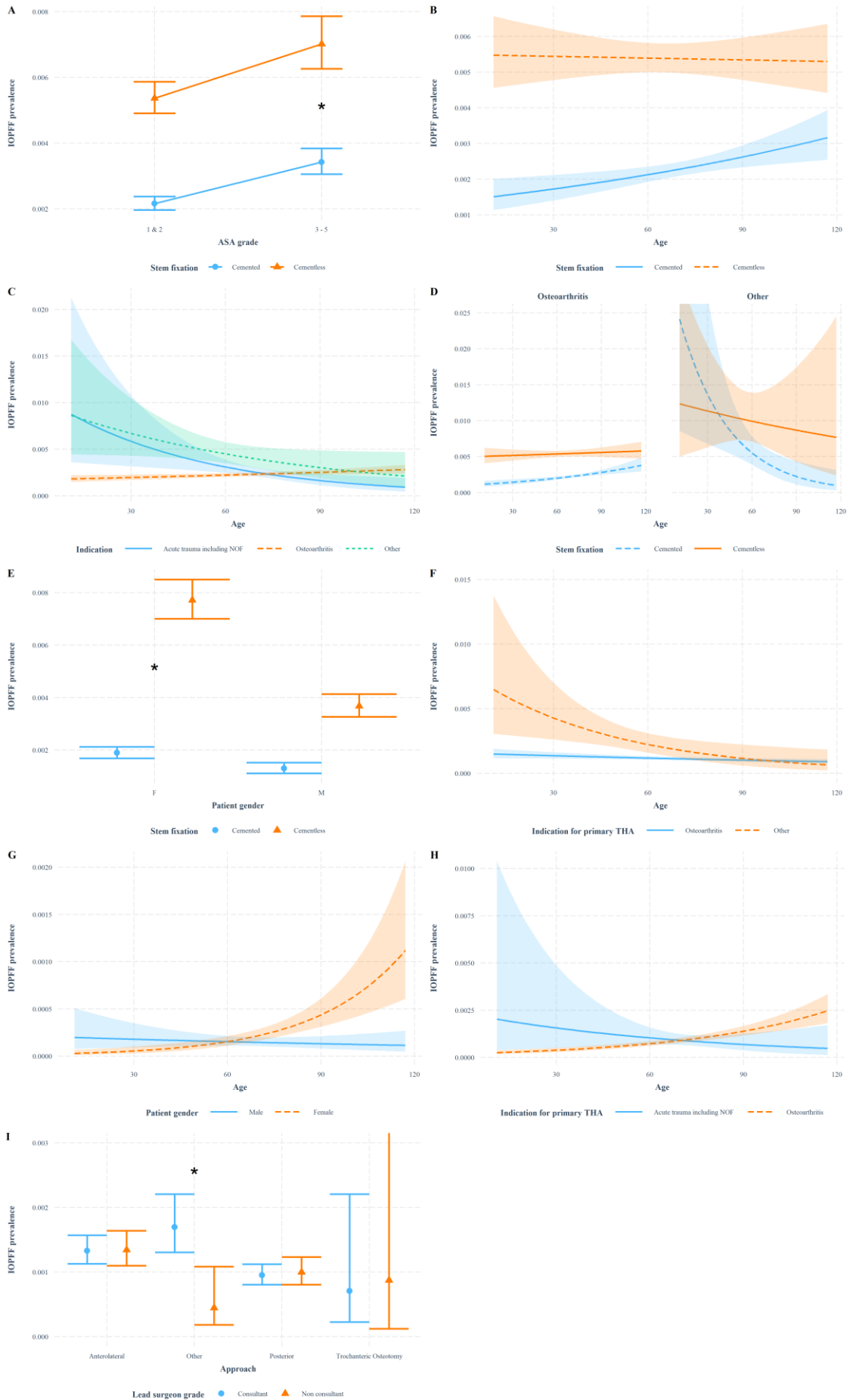
354 **Table 5.** Fixed effects of statistically significant interaction terms.

Multivariable model outcome	Interaction covariates	Interaction level	RR	p
Any IOPFF	ASA : Fixation	ASA grade 3 to 5 : Cementless stem	0.83	<0.01
Any IOPFF	Age : Fixation	Age increase of one year : Cementless stem	0.99	<0.01
Any IOPFF	Age : Indication	Age increase of one year : Acute trauma including NOF	0.96	<0.01
Any IOPFF	Age : Indication	Age increase of one year : Other	0.96	<0.01
Any IOPFF	Age : Indication : Fixation	Age increase of one year : Other: Cementless stem	0.08	<0.01
Calcar crack	gender : Fixation	Female gender : Cementless stem	1.44	<0.01
Calcar crack	Age : Indication	Age increase of one year : Other	0.96	<0.01
Shaft fracture	Age : Gender	Age increase of one year : Female gender	1.04	<0.01
Trochanteric fracture	Age : Indication	Age increase of one year : Acute trauma including NOF	0.95	<0.01
Trochanteric fracture	leadsurgeon : approach	Non Consultant : Other	0.25	<0.01

Note: IOPFF indicates intraoperative periprosthetic femoral fracture, RR indicates relative risk associated with interaction term, p indicates the significance of the interaction term in the multivariable model indicated in IOPFF type, THA indicates total hip arthroplasty, CGS indicates computer guided surgery, ASA indicated American society of anaesthesiologists and NOF indicates neck of femur fracture

355

356 **Figure 1:** Panel plot demonstrating effect of significant interaction terms on the predicted incidence
357 of intraoperative periprosthetic femoral fracture during primary total hip arthroplasty.



359 Note: Figure 1(A) Demonstrates the interaction of ASA grade and stem fixation on risk of IOPFF risk.
360 Figure 1(B) demonstrates the interaction of patient age and stem fixation on predicted prevalence of
361 any IOPFF.

362 Figure 1(C) Demonstrates the interaction of patient age and indication for primary surgery on
363 predicted prevalence of anyIOPFF. only diagnoses which reached statistical significance and
364 osteoarthritis (reference) are displayed.

365 Figure 1(D) Demonstrates the interaction of patient age, indication for primary surgery and stem
366 fixation on predicted prevalence of any IOPFF. only diagnoses which reached statistical significance
367 and osteoarthritis (reference) are displayed.

368 Figure 1(E) Demonstrates the interaction of patient gender and stem fixation on predicted prevalence
369 of calcar crack.

370 Figure 1(F) Demonstrates the interaction of patient age and indication for surgery on predicted
371 prevalence of calcar crack. only diagnoses which reached statistical significance and osteoarthritis
372 (reference) are displayed.

373 Figure 1(G) Demonstrates the interaction of patient age and gender on predicted prevalence of shaft
374 fracture.

375 Figure 1(H) Demonstrates the interaction of patient age and indication for surgery on predicted
376 prevalence of trochanteric fracture.

377 Figure 1(I) Demonstrates the interaction of lead surgeon grade and surgical approach on predicted
378 prevalence of trochanteric fracture.

379 * denotes the level of categorical variable at which the interaction reaches significance

Table 6. Relative risk of IOPFF in a typical OA patient undergoing THA using a selection of worst vs best modifiable risk factors.

Fracture type	RR	(95% CI)	p
All fractures	4.29	(3.34 - 5.51)	<0.001*
Calcar crack	7.72	(5.65 - 10.50)	<0.001*
Shaft fracture	2.93	(1.17 - 7.32)	0.02
Trochanteric	1.64	(1.02 - 2.64)	0.042

Note: Best scenario (Cemented stem, posterior approach and computer guided surgery), worst scenario (Cementless stem, Anterolateral or other approach without computer guided surgery). RR Relative risk, CI confidence interval, * p<0.01

380

381 **Appendix**

382 A.1:

A priori clinically relevant interactions tested

age : gender
gender : stem sixation
ASA : stem sixation
ASA : lead surgeon grade
ASA : lead surgeon grade : stem sixation
age : stem sixation
age : gender : stem sixation
age : indication
age : indication : stem sixation
cgs : age
cgs : indication
cgs : age : indication
cgs : side
cgs : lead surgeon grade
cgs : approach
cgs : stem sixation
cgs : stem sixation : organisation type
lead surgeon grade : organisation
lead surgeon grade : approach
side : approach *
side : surgeon *
side : surgeon : approach *

Note: THA indicates total hip arthroplasty, CGS indicates computer guided surgery, ASA indicated American society of anaesthesiologists. * denotes interaction only tested on multivariable model predicting risk of any intraoperative fracture