



■ ARTHROPLASTY

The incidence of venous thromboembolism in total joint replacement during COVID-19 pandemic

HAS LOCKDOWN HAD AN INFLUENCE?

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Aims

As the first wave of the COVID-19 pandemic began to dip, restarting elective orthopaedics became a challenge. Protocols including surgery at 'green' sites, self-isolation for 14 days, and COVID-19 testing were developed to minimize the risk of transmission. In this study, we look at risk effects of 14-day self-isolation on the incidence of venous thromboembolism (VTE) in our green site hospital among patients undergoing total joint replacement (TJR).

Methods

This retrospective cohort study included 50 patients who underwent TJR. Basic demographic data was collected including, age, sex, American Society of Anesthesiologists (ASA) grade, body mass index (BMI), type of surgery, and complications at two and four weeks. Univariate and multivariate analysis were used to identify risk factors associated with an increased risk of VTE.

Results

A total of 50 patients were included in our study, with 24 males and 26 females. The mean age was 67.86 (SD 11.803). Overall, 8% of patients suffered a VTE complication; symptomatic non-fatal pulmonary embolism was confirmed in 6% of patients (n = 3) as an inpatient, and symptomatic deep vein thrombosis was diagnosed in 2% of patients (n = 1) within two weeks of their operation. All patients were found to be female (p < 0.001), had a BMI > 30 (p = 0.317), and were immobile prior to their operation using walking aids (p = 0.016).

Conclusion

The incidence we report is much higher than the reported incidence in the literature, which we believe is related to the 14-day self-isolation period and immobility prior to their operation. We recommend that all patients undergoing TJR that require a period of self-isolation, are pre-assessed prior to self-isolation for their risk of VTE, potentially using mechanical and chemical prophylaxis to reduce the likelihood of developing VTE.

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Introduction

The COVID-19 outbreak was declared a pandemic by the World Health Organization on 11 March 2020.¹ Governments were urged to take aggressive action to limit the spread, implementing measures such as lockdown. Since then, the pandemic has had a huge impact on the ability of health-care professionals to deliver services to

non-COVID-19 patients, such as elective operating in orthopaedics.

As the peak of the pandemic passed, government restrictions started to lift, and elective operating services slowly resumed. The British Orthopaedic Association (BOA) and NHS England set out a three phase guideline to allow a phased return of the much needed elective orthopaedic services.^{2,3} Some of the provisions include a 14-day

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Table I. Baseline characteristics and study outcomes for all patients.

Characteristic	Total, n	VTE complications,	p-value
		n (%)	
Age, yrs			0.308*
< 70	28	1 (2)	
> 70	22	3 (6)	
Sex			< 0.001*†
Male	24	0 (0)	
Female	26	4 (8)	
Procedure			
THA	21	2 (4)	0.638‡
TKA	19	0 (0)	0.285‡
Revision THA	6	1 (2)	0.411‡
Revision TKA	3	1 (2)	0.291‡
Other	1	0 (0)	> 0.999‡
ASA grade			0.246*
I	6	0 (0)	
II	30	2 (4)	
III	14	2 (4)	
IV	0	0 (0)	
Anaesthesia			> 0.999*
Spinal	20	2 (4)	
GA	30	2 (4)	
BMI			0.317*§
< 18 kg/m ²	0	0 (0)	
18 kg/m ² to 23 kg/m ²	4	0 (0)	
23 kg/m ² to 30 kg/m ²	25	1 (2)	
> 30 kg/m ²	21	3 (6)	
Smoking status			> 0.999*
Smoker	6	0 (0)	
Non-smoker	44	4 (8)	
Mobility status			0.016*†
Walks unaided	31	0 (0)	
One stick	15	3 (6)	
Two sticks	3	0 (0)	
Frame	1	1 (2)	
VTE prophylaxis compliance			> 0.999*
Yes	46	4 (8)	
No	0	0 (0)	
Self-isolation after surgery			0.538*
Yes	46	4 (8)	
No	4	0 (0)	

*Chi-squared test.

†Statistically significant.

‡Fisher's exact test.

§BMI < 30 kg/m² vs > 30 kg/m².

ASA, American Society of Anesthesiologists; BMI, body mass index; GA, general anaesthesia; THA, total hip arthroplasty; TKA, total knee arthroplasty; VTE, venous thromboembolism

period of self-isolation prior to surgery, preoperative testing, and surgery at a clean, 'green', non-COVID-19 site.^{2,3} The 'green' elective areas are for patients who have self-isolated in their homes for 14 days prior to admission. They will have been screened and no COVID-19 detected.

Venous thromboembolism (VTE) is a recognized complication following total joint replacement (TJR).⁴ Patients undergoing TJR are at a much higher risk as all

the pathophysiological processes of Virchow's triad⁴ (vascular endothelial damage, stasis of blood flow, and hypercoagulability of blood) are present.⁵ The incidence of deep vein thrombosis (DVT) is fairly common, being reported between 40% to 60% after major orthopaedic surgery.⁶ In comparison, fatal pulmonary embolism (PE) is far less common, with an incidence of 2% to 3% after elective hip arthroplasty.⁶

With the implementation of lockdown and new provisions during this pandemic, such as a 14-day self-isolation prior to surgery, patients are undoubtedly becoming less mobile, suggesting a potential increased risk of VTE. We hypothesize that a preoperative self-isolation period, to minimize risk of contracting COVID-19, increases the incidence of VTE in patients undergoing TJR. In this article we present our data on restarting elective TJR work at our 'green' site hospital and report the outcomes, particularly looking to see if there is an increased rate of VTE.

Methods

Study design. This retrospective case series included all patients who had undergone TJR in our 'green' site hospital in Essex, UK, between 18 May 2020 and 19 July 2020. Inclusion criteria were as follows: patient had a TJR procedure; patient had self-isolated for 14 days prior to admission for the procedure; patient had been informed to self-isolate for 14 days after discharge from the procedure; patient was followed up for 30 days following discharge. Exclusion criteria were as follows; patient had a non-TJR procedure; patient was not able to self-isolate before the procedure.

Overall, 62 patients were eligible for our study. However, two were lost to follow-up, and ten patients had their surgery cancelled due to not being fit for surgery at the green site (six positive for methicillin-susceptible *Staphylococcus aureus*; two cancelled due to previous intensive therapy unit admissions; one suffered diarrhoea and vomiting on the morning of surgery; one was over the body mass index (BMI) limit for the green site policy).

Demographics. Our cohort was equally distributed with regards to age (56% < 70 years (n = 28), 44% > 70 years (n = 22)) and this was equivocal for sex (48% male, 52% female). There was statistical significance in the number of females who developed VTE (8%, n = 4; p < 0.001, chi-squared test). There was no significant difference in the type of procedure performed, ASA grade, anaesthesia type, BMI, or smoking status.

A total of 50 patients were ultimately included (24 males and 26 females). Of these, 21 patients had a total hip arthroplasty (THA), 19 patients had a total knee arthroplasty (TKA), six patients had a revision THA, three patients had a revision TKR, and one patient had a partial knee arthroplasty (patellofemoral arthroplasty). The mean age was 67.86 years (SD 11.80). Demographics are shown in Table I.

Table II. Risk factor profile in patients who developed venous thromboembolism.

Patient	Procedure	Complication	Comorbidities	VTE risk factors
1	THA	Pulmonary embolism	Osteoarthritis, hypercholesterolaemia, hypertension, peripheral vascular disease, trochanteric bursitis.	Female, obesity, peripheral vascular disease
2	Revision THA	Pulmonary embolism	Osteoporosis, angina, hypertension	Female, obesity
3	Revision TKA	Pulmonary embolism	N/A	Female, obesity
4	THA	Deep vein thrombosis	N/A	Female, obesity

N/A, not applicable; THA, total hip arthroplasty; TKA, total knee arthroplasty; VTE, venous thromboembolism

Data collection. Data were collected by surgical care practitioners using a predesigned pro forma and reviewed by a lead orthopaedic consultant (attending) (JT) and registrar (resident) (SAK).

The following data was collected: patient demographics (age, sex, type of surgery, American Society of Anesthesiologists (ASA) grade,⁷ BMI; preoperative factors (comorbidities, smoking status, mobility status, reverse transcription polymerase chain reaction (RT-PCR), SARS-CoV-2 swab status, chest CT result (if applicable)); operative factors (type of surgery performed, length of surgery, complications during surgery); postoperative factors (postoperative complications, type of VTE prophylaxis, period of self-isolation after the surgery, final outcome after 30 days).

Patients were followed up face-to-face in the community by the community nursing team. They were then subsequently followed up at 30 days and six weeks virtually in a telephone clinic.

Ethics committee approval was not required as this study was considered a necessary review of service. None of the authors received any financial support and do not have any conflicts of interest to declare.

Statistical analysis. Independent-samples *t*-tests were used to compare study outcomes found to be normally distributed, while the Mann-Whitney U test was used for continuous outcomes found not to be normally distributed. Categorical outcomes were compared using the chi-squared and Fisher's exact test. Statistical significance was set at a *p*-value < 0.05 for all analyses and all statistical analyses were performed using SPSS v. 26 (IBM, Armonk, New York, USA).

Results

VTE complications. In total, 8% of patients developed a VTE complication; symptomatic non-fatal PE was confirmed in 6% of patients (*n* = 3) as an inpatient, and symptomatic DVT was diagnosed in 2% of patients (*n* = 1) within two weeks of their operation. No patients were confirmed to develop concomitant DVT and PE. All four of these patients went on to have a treatment dose anticoagulation and were referred to the medical anticoagulation team for further review.

Two other patients (4%) complained of a painful calf within two weeks of their operation and sought medical

advice at the emergency department. Both patients had a negative Doppler ultrasound.

Other complications. Two patients complained of oozy wounds; one settled with dressings and review with the community nursing team; the other sought general practitioner (GP) advice and was prescribed prophylactic antibiotics. One patient complained of shortness of breath and tachycardia and was found to have a new diagnosis of pheochromocytoma.

Self-isolation. There was a 100% compliance rate with self-isolation for 14 days prior to admission to hospital. There was a 92% compliance rate with self-isolation after discharge from the hospital; two patients had to seek medical advice regarding swollen calves, one patient sought advice from her GP regarding an oozy wound, and the final patient was transferred following an incidental finding of a pheochromocytoma. All four patients had negative RT-PCR SARS-CoV-2 swabs after breaking the isolation period. We were unable to collect data regarding the mobility status during the self-isolation period.

Mobility status. Over half of our patients walked unaided (62%, *n* = 31) whereas the remaining 38% required walking aids. There was statistical significance between those who required aids versus those who did not (*p* = 0.016, chi-squared test) for the development of VTE. However, the difference between using one stick and other forms of aids did not reach statistical significance (*p* = 0.016, chi-squared test).

Comorbidities. Only two of the patients who developed VTE had significant comorbidities (4%). Only one of these patients had a comorbidity recognized as a significant risk factor in the literature for development of VTE. The comorbidities are outlined in Table II.

Anticoagulation. All patients were administered VTE prophylaxis postoperatively, both chemical (low molecular weight heparin or aspirin, depending on surgeon preference) and mechanical (graduated compression stockings and intermittent pneumatic compression devices). Patients who had a THA-related procedure were given four weeks' worth of prophylaxis, whereas patients who had a TKA-related procedure were given two weeks' worth of prophylaxis. Patients reported a 100% compliance with taking their VTE prophylaxis medication. All patients who developed a VTE were on low molecular weight heparin.

Discussion

In our study, the incidence of VTE was 8% ($n = 4$), clinical DVT was 2% ($n = 1$), and the incidence of non-fatal PE was 6% ($n = 3$) following TJR. Our findings are significantly higher than reported in the literature.

O'Reilly et al⁸ reported an incidence of 1.9% for symptomatic non-fatal PE in 5,999 patients after orthopaedic elective surgery. Another group from Norway reported a cumulative incidence of 2.7% for symptomatic VTE, of which 1.1% developed a PE and 1.5% developed a DVT.⁹ A group in California looked at over 43,000 patients over a four-year period and reported a cumulative incidence of 2.1% and 2.8% of VTE after THA and TKA, respectively.¹⁰ Douketis et al¹¹ performed a meta-analysis of over 7,000 cases and reported an incidence of 3.2% for symptomatic VTE three months after TKA or THA.

The significant difference in incidence reporting favours the notion that the effect of self-isolation has an impact. Prolonged immobility is a recognized risk factor for developing VTE, due to the venous stasis proposed by Rudolph Virchow.¹¹ The odds ratio (OR) is significantly higher (> 10) if this in conjunction with strong risk factors, such as undergoing a THA or TKA.⁵ All of our patients had to undergo a 14-day period of self-isolation, which limited the amount of outdoor exposure and exercise they were able to do. In addition, the majority of these patients endured a significant deterioration in quality of life and pain as a result of cancelled and rescheduled operations due to the pandemic.¹² This will have worsened their arthritis, made their immobility worse, and started a vicious cycle, further increasing their risk of developing VTE.

Patients awaiting TJR usually have problems mobilizing, with their arthritis pain reducing their mobility or patients requiring walking aids to mobilize. The majority of our patients were independently mobile. However, 38% required some form of walking aid to mobilize. Those using walking aids had a statistically significant increased risk of VTE in our study population ($p = 0.016$, chi-squared test). All of the patients that developed VTE had some restricted mobility and required an aide. This suggests that reduced mobility is an additional risk factor for the development of VTE. This may be compounded by having to self-isolate, and therefore cause these patients to have a further reduction in their mobility in the self-isolation period. This further strengthens our hypothesis that immobility has had an influence, as demonstrated by the increased OR in the immobile patient.⁵

All patients who developed VTE were female. There has been research to suggest women are more prone to VTE due to pregnancy in the young patient, menopause, and hormone replacement therapy (HRT) in the older patient.¹³ Two of the patients were on HRT at some point prior to the surgery, but not in the run-up.

Obesity has been shown to be a risk factor for the development of VTE.¹⁴ The individuals who developed a VTE had a BMI > 29.9 kg/m², classing them as obese. Stein et al¹⁵ showed that the relative risk for developing VTE was much higher in females with a BMI > 30 kg/m², and the greatest impact was in women < 40 years old. Studies have also shown that women were more likely than men to change their weight prior to TJR, and younger patients were more likely to gain weight than older patients both before and after THA and TKA.¹⁶ We hypothesize this phenomenon to be much greater during self-isolation due to the immobility, as described above.

Ageing has another negative effect on endothelial dysfunction and venous insufficiency, leading to increased incidence of VTE.¹⁷ Patients over the age of 40 are at significantly increased risk compared with younger patients. This risk is estimated to be double with each subsequent decade.⁵ These patients become more immobile as they age, adding another major risk factor to their predisposition of developing VTE. All of our patients who developed a VTE event were greater than 40, increasing their risk for VTE.

Another variable, which we were unable to measure, was the preoperative level of hydration of the patients. Hydration has played an important role in preventing VTE prior to major surgery, due to the increased blood viscosity.¹⁸ Many of our patients had not had any oral fluids for almost 12 hours prior to admission, and a few of our patients had to wait longer to go down to theatre for their operation. The dehydration was, occasionally, exacerbated by lack of intravenous fluid prescription.

From this data, we can see that there is a significant increase in VTE events, with the only altered variable being immobility during the 14-day self-isolation following TJR. Patients are encouraged to mobilize after their operation as much as possible which is guided by physiotherapy. Unfortunately, this service is not available at home for patients and there may be a higher tendency toward sedentary activities rather than active mobilization.

Research has shown that standardized home therapy programmes significantly reduce the likelihood of VTE complications.¹⁹ Simple active ankle movements have been shown to increase maximum venous outflow and reduce blood rheology, which may reduce the development of VTE.²⁰ These exercises can be performed at home without supervision and will also work as a weight loss incentive. In addition, initiation of mechanical prophylaxis (in the form of graduated compression stockings and intermittent pneumatic compression devices) have been shown to greatly reduce VTE development in patients > 70 years old with a hip fracture.²¹ We therefore propose to initiate a home physiotherapy prehab programme with mechanical prophylaxis, which will be given to patients when they are informed of a date for their procedure.

There is some debate as to whether starting preoperative chemical prophylaxis can reduce the risk of developing VTE. Many authors have reported no advantage initiating chemical prophylaxis preoperatively, with the incidence of VTE being equally distributed in both groups.^{22,23} In fact, Borgen et al²³ and Wein et al²⁴ reported a higher bleeding risk intra- and postoperatively. However, neither of the authors used low-dose aspirin as an anticoagulant, which has been shown to have a lower bleeding risk compared to other aggressive anticoagulants.²⁵

Though this study offers some valuable data during the COVID-19 pandemic, it does not provide conclusive evidence that self-isolation has directly increased the incidence of VTE during this period due to a number of residual confounding factors. For example, female sex and obesity are independent risk factors. As such, further large randomized controlled trials are required to determine this correlation and to assess the effectiveness of preoperative administration of chemical and mechanical thromboprophylaxis.

Our sample size was lower than other studies investigating VTE incidence, given that this remains a relatively rare complication. This was due to the slow restart of elective services during this pandemic in a smaller green site hospital. Many patients have also declined to continue with their planned surgeries due to the risk of COVID-19.¹²

Restarting elective orthopaedic services during the pandemic has been challenging so far. Through the development of safe protocols, we have fought the first battle to keep our patients safe from COVID-19. However, our research demonstrates an increased incidence of VTE in patients undergoing elective TJR during the pandemic. This can be attributed to a range of variables, which have shown to increase the risk of developing VTE — the most interesting and concerning being the 14-day self-isolation period prior to surgery and increased immobility prior to surgery.

From our study population, immobile females who use a walking aid carry the greatest risk of developing a VTE. As our protocols for elective surgery have changed to enable a restart and keep patients safe from the risk of COVID-19, we would advocate that all patients undergoing TJR, who require a period of self-isolation, are pre-assessed prior to self-isolation for their risk of VTE. If they are in a moderate- to high-risk group, we recommend they be offered a minimum of mechanical prophylaxis during self-isolation, advised on general measures of hydration, and maintain their usual levels of mobility. Those in the highest risk group should also be considered for mechanical and chemical prophylaxis in combination to further reduce their relative VTE risk.

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- P. Logan: Collected and collated the data, Performed the statistical analysis, Contributed to production of the final manuscript.
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Ethical review statement

- Ethics committee approval was not required as this study was considered a necessary review of service.

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