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Exploring factors associated with failure of totally implanted vascular access devices in a regional and rural health service: a retrospective case–control study

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ABSTRACT

Background The assessment and management of totally implanted vascular access devices (TIVAD) prior to the administration of medications/fluids are vital to ensuring the risk of harm is mitigated. While numerous guidelines exist for the insertion and management of TIVAD, the level of evidence and external validity to support these guidelines is lacking.

Objectives The purpose of this study was to identify factors associated with suboptimal TIVAD placement and with failure of TIVAD.

Methods A retrospective case–control study (n=80) was conducted at a regional hospital and health service in Australia. Binomial logistic regression analysis was performed using a backward selection approach to establish variables associated suboptimal TIVAD placement and with TIVAD failure.

Findings Significant associations were identified between the patient's primary diagnosis and suboptimal TIVAD insertion. Specifically, a prior diagnosis of breast cancer was associated with a decreased probability of optimal TIVAD tip placement (OR=0.236 (95% CI 0.058 to 0.960), p=0.044). A statistically significant association between TIVAD failure and the log of the heparinised saline flush rate and rate of undocumented flushes was also established. Further research is needed to identify and assess whether modification of these variables improves initial totally implantable venous access ports placement and risk of subsequent failure.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Totally implanted vascular access devices (TIVADs) play a crucial role in providing long-term venous access to various medical treatments, including chemotherapy. While TIVADs offer several advantages such as improved patient safety and quality of life, they are prone to occlusion and failure, which can interrupt treatment and affect clinical outcomes. Previous research has identified various risk factors for TIVAD failure, including mechanical obstruction, thrombotic obstruction and catheter-related thrombosis. Additionally, guidelines exist for the insertion and management of TIVADs; however, the level of evidence supporting these guidelines is limited.

WHAT THIS STUDY ADDS

⇒ This retrospective case–control study investigated factors associated with suboptimal TIVAD placement and TIVAD failure in a regional hospital and health service. The study found a significant association between a patient's primary diagnosis, specifically breast cancer and suboptimal TIVAD tip placement. Additionally, the study identified increased flushing with heparinised saline and poor documentation of flushes as significant factors associated with TIVAD failure.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings of this study provide valuable insights into factors influencing TIVAD placement and failure. Specifically, the association between breast cancer diagnosis and suboptimal TIVAD tip placement suggests a need for further research to identify modifiable risk factors for placement difficulties, particularly in breast cancer patients. Moreover, the association between TIVAD failure and increased flushing with heparinised saline underscores the need for reconsideration of flushing protocols, as well as the importance of adequate documentation in clinical practice. These findings may contribute to improved patient outcomes and healthcare resource management in the management of TIVADs.

BACKGROUND

Over the last decade, many changes have occurred in oncology with new systemic anticancer treatment (SACT) combinations, more complex application schemes and longer treatment periods. Repeated and prolonged durations of therapy coupled with the properties (irritants and vesicants) of most chemotherapy drugs increase the likelihood of difficult intravenous access, adding considerable challenges for both the patient and clinician.[1] Central venous access devices (CVADs) have mitigated the problem of vascular access. Totally implanted vascular access devices (TIVADs) are effective for long-term venous access and improved patient safety. Besides administering SACT, TIVADs are used to administer blood, blood products and nutrition and also can be used to withdraw blood from.[2] Because TIVADs are situated subcutaneously, they do not affect range

Table 1 Binary and Categorical Variables

Variable	Categories	Frequencies
Arm side	0=Right 1=Left	53 (66.25%) 27 (33.75%)
Diagnosis	0=Breast cancer 1=Colorectal cancer 2=Other	37 (46.25%) 24 (30.00%) 19 (23.75%)
Sex	0=Male 1=Female	20 (25.00%) 60 (75.00%)
Brand	0=Bard 1=Smiths Medical	50 (63.29%) 29 (36.71%)
Successful placement	0=No 1=Yes	38 (47.50%) 42 (52.50%)
TIVAD failure	0=No 1=Yes	40 (50.00%) 40 (50.00%)

Continuous variables

Variable	No. of observation	Median	Mean	SD
Log of heparinised saline flush rate	68	−2.20	−2.26	1.43
Log of not documented rate	68	−1.91	−1.90	1.11

of motion or impede daily activities,[3] hence they result in better patient quality of life (QOL).[4]

At the author's clinical site, an increase in the number of occluded TIVAD requiring assessment through portogram was observed. A portogram is a fluoroscopic examination to evaluate a TIVAD or other implanted venous access device for patency.[3] These occlusions interrupt and delay treatment for the underlying disease and thereby affect clinical outcomes.

TIVAD occlusion occurs in 14%–36% of patients within 1–2 years of catheter placement.[5] A TIVAD occlusion can be partial, in that blood cannot be aspirated but infusion through the catheter is possible, or complete, with neither aspiration nor infusion possible A TIVAD occlusion can arise from mechanical obstruction,[2] precipitation of drugs or parenteral nutrition preparations or from thrombotic obstruction.[6] Catheter-related thrombosis in long-term TICVADS occurs in up to 50% of children and 66% of adults with a long-term TIVAD and can cause long-term vascular complications.[7] There are several recognised risk factors for catheter-related thrombosis, such as TIVAD biocompatibility, catheter tip position, insertion side, site of insertion, thrombophilic abnormalities and catheter-related infections.[5] Catheters can also become occluded secondary to a thrombotic process, such as a fibrin sheath around the catheter tip, an intraluminal blood clot, or a venous thrombosis, which can occur separately or in combination.[8] A fibrin sheath is one of the most common causes of thrombotic obstruction. It can occur within 24 hours after CVAD placement and usually develops within 2 weeks.

The position of the catheter tip in the vascular system is an important risk factor for the development of catheter-related thrombosis.[9] The incidence of catheter-related thrombosis is higher in patients in whom the catheter tip is placed in the brachiocephalic veins or proximal superior vena cava (SVC) as compared with the distal SVC/right atrial junction.[2 6]

To prevent thrombotic catheter occlusions, most health organisations that use long-term TIVAD have standard protocols for the method and frequency of flushing the catheter. However, there is insufficient evidence on which to base universal guidelines for these practices, specifically regarding the type of solution used (10 U/mL heparin vs 100 U/mL heparin vs 0.9% Sodium Chloride) and the frequency of flushing the catheter. Evidence suggests that the use of heparin as a locking solution for the prevention of thrombotic occlusions is not recommended and that locking with 0.9% sodium chloride is just as effective.[10–12]

While numerous guidelines exist for the insertion and management of TIVAD,[13] the level of evidence and external validity to support these guidelines is lacking. Identifying factors associated with TIVAD failure and working towards their elimination may positively benefit patient QOL, clinical outcomes and health system resourcing. The aim of this study was to explore factors associated with suboptimal TIVAD placement and TIVAD occlusion in a regional hospital and health service.

METHODS

Study design

A retrospective case–control study was performed on patients who had TIVAD in situ during 2019–2020, including patients who had their TIVAD inserted prior to this period.

Participants

The case group consisted of all patients who had a TIVAD inserted within the health service and who developed a

Table 2 Logistic regression model for variables affecting TIVAP tip placement

Variable	OR	95% CI	P value
Arm side	0.513	(0.175 to1.501)	0.223
Diagnosis			
0	0.236	(0.058 to 0.960)	0.044
1	1.430	(0.353 to 5.798)	0.616
Sex	2.771	(0.664 to 11.571)	0.162
Manufacturer			
1	1.988	(0.678 to 5.831)	0.211
		LR χ^2(df=5)	11.33
		P value	0.0452
		PseudoR^2	0.1038
		No. of observations	79

TIVAP, totally implantable venous access ports.

catheter occlusion requiring a diagnostic portogram. The control group consisted of patients with TIVAD during the same period, who did not develop occlusion evidenced by requiring portogram.

Patients aged less than 18 years old during the study period were excluded. In cases where patients had required multiple portogram studies during the study period, only the first portogram data within the defined period was included.

Patient and public involvement

As this was a retrospective study, it was not possible or appropriate to involve patients or the public in the design or conduct of the project.

Data collection

The variables collected were determined by a previously conducted (unpublished) rapid review by members of the investigation team and based on a validated evidence synthesis methodology.[14] Datapoints for participants age, diagnosis, evidence of TIVAD insertion within a local facility, as well as evidence of TIVAD being performed, were also collected to determine eligibility for inclusion in the study (as per inclusion criteria) and which arm they were to be included in.

Data were retrieved from enterprise reporting systems, such as a statewide radiology information reporting system, the Emergency Department Information System, Operating Room Management Information System, Oncology Information Management System, Medical Records and Enterprise Picture Archiving and Commination Systems.

TIVAD postplacement imaging was retrospectively reviewed by a consultant radiologist to determine relevant factors relating to imaging criteria. All patients had either or both a postprocedural chest X-ray and/or an intraprocedural image intensifier screenshot. The radiologists were blinded to all patient data including whether the image was a case or a control in the study.

All data were collected and cleaned in Microsoft Excel and statistical analysis was performed in Stata V.17.0.

RESULTS

Two logistic regression models were developed to establish factors affecting (a) initial success of TIVAD placement and (b) failure of the TIVAD after insertion. Success for (a) was defined as a binary variable (successful placement) determined by imaging of the tip location, where placement was successful if the catheter tip was situated in the mid-SVC to lower-SVC. TIVAD failure in (b) was determined by whether a TIVAD required imaging (a port-a-gram) to reassess location of the device, indicating that the device had lost patency.

Descriptive statistics

Descriptive statistics for the variables included in the final models are provided in table 1. Outlier observations were removed in the analysis of (b) if the TIVAD lasted less than 14 days before failing. The cut-off of 14 days was chosen based on the undue leverage these observations had on the residuals of the initial model in which they were included.

The median number of days to failure was 99, with the minimum number of days being 4 and the maximum number of days being 1715.

Inferential statistics

Categorical variables were implemented in the regression model using the dummy coding method. Categorical variables with high cardinality were reduced in dimension by collapsing categories with lower frequencies of observations into a broader category. Variables for which data were missing were removed using listwise deletion under the assumption that data were missing completely at random.

A logistic model was fit for all explanatory variables for which data was collected. Backwards elimination was performed with a p value cut-off of 0.25 for elimination. Models were compared and reduced based on the results of log-ratio tests, Akaike information criterion (AIC) and Bayesian information criterion (BIC).

The OR for the variable Arm Side is the odds of a right-sided insertion compared with left sided, the OR for the diagnosis variable is compared with patients with diagnoses other than breast or colorectal cancer, the OR for the sex variable is compared with males and the OR for manufacturer is compared with the Bard devices.

Results from the logistic regression model are presented in table 2.

A diagnosis of breast cancer was associated with a statistically significant decrease in the odds of optimal TIVAD tip placement compared with patients with other diagnoses at the = 0.05 level, OR=0.236 (p=0.04). Arm side, sex and manufacturer were all statistically insignificant factors at the chosen p value cut-off, however, inclusion

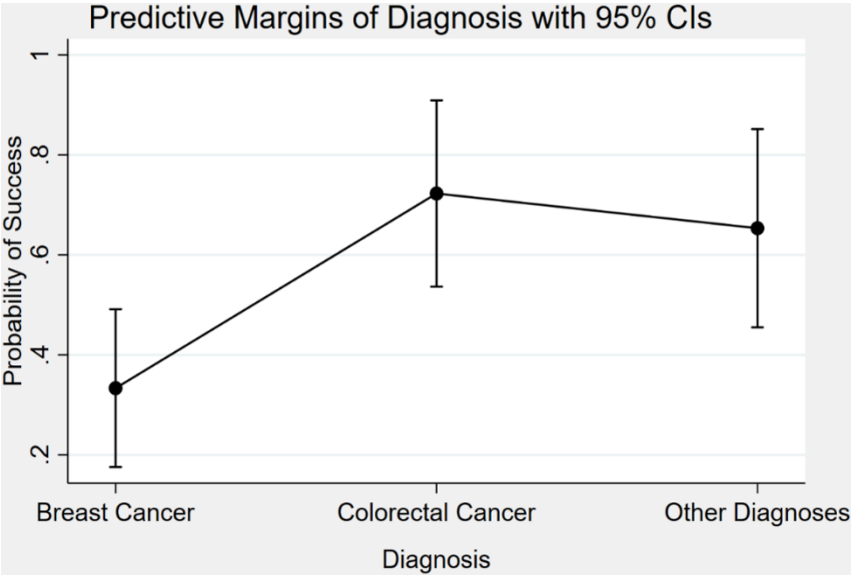

Figure 1 Predictive margins plot comparing probability of successful tip placement across diagnoses.

of these variables in the model improved overall model fit as assessed by AIC and BIC. The predictive margins plot in figure 1 demonstrate the probability of successful insertion for the categories of the diagnosis variable with their 95% CI.

Failure of the TIVAD after insertion was the second endpoint for this research. A logistic regression model was produced using the same modelling techniques used in the analysis of (a) to assess factors associated with TIVAD failure. The dependent variable for this analysis was whether patients received a port-a-gram, indicating that the TIVAD had failed. Rate variables are presented as the number of events occurring per week. The natural logarithm of the rates was used in the analysis due the data following an exponential frequency distribution.

Results from the logistic regression model are provided in table 3.

Logistic regression for factors affecting TIVAD failure produces a model with two statistically significant independent variables at the α=0.05 level; the log of the heparinised flush rate (OR 1.977, 95% CI (1.243 to 3.143), p=0.004), and the log of the non-documented flush rate (OR 2.179, 95% CI (1.176 to 4.036), p=0.004). Calculating the marginal effects for this result shows that for every 1% increase in the heparinised saline flush rate the probability of TIVAD failure increases by 0.001. Similarly, a 1% increase in the rate of non-documented flushes increases the probability of failure by 0.001. Predictive margins plots were produced for both statistically significant independent variables (see figures 2 and 3).

DISCUSSION

The Kaplan-Meier survival curve (in figure 4) shows that half of the TIVAD that failed in the study failed before 100 days had elapsed and a quarter had failed just 26.5 days after insertion. The short time to failure for these devices which are often needed for up to years at a time poses a large burden on both patients and the healthcare system. Identifying factors that lead to suboptimal placement and to failure of these devices is, therefore, important for individual patients and to the broader system.

The regression model for the first outcome of this retrospective study demonstrated an association between a patient's primary diagnosis and the optimal placement of their TIVAD during initial insertion. Patients with breast cancer were observed to have a lower probability of optimal tip placement during initial insertion within

Table 3 Logistic regression model for variables affecting TIVAP patency

Variable	OR	95% CI	P value
Log of heparinised saline flush rate	1.977	(1.243 to 3.143)	0.004
Log of the non-documented flush rate	2.179	(1.176 to 4.036)	0.013
		LR χ^2 (df=2)	23.25
		P value	<0.001
		Pseudo R^2	0.2473
		No. of observations	68

TIVAP, totally implantable venous access ports.

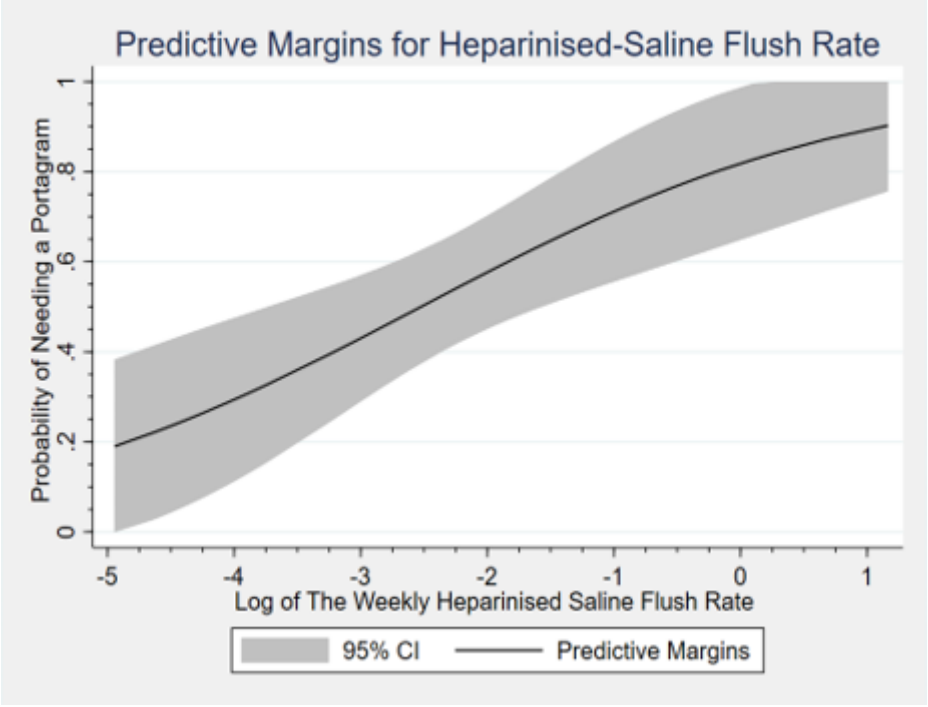

Figure 2 Predictive margins plot for probability of failure as a function of the log of the heparinised flush weekly rate.

this cohort. The cause of this difference was not explored as part of this study; however, the result may suggest that diseases anatomically removed from the location of insertion increase the probability of optimal insertion. This study did not record the specific details of the patient's breast cancer diagnosis. The relation of the cancer to the side of insertion, the anatomical location of the cancer, axillary node involvement and clearance, the presence of metastatic disease, prior surgeries such as mastectomy, as well as type of cancer are all factors that may have impacted the difficulty of insertion, choice of insertion side and insertion technique used. External factors may also have contributed to this result, such as operator comfortability with the side of insertion and layout of the operating theatre facilitating less optimal insertion. Optimal tip placement is clinically important for the patient and the healthcare service, as less optimal placement locations are associated with thrombus formation, cardiac arrhythmias

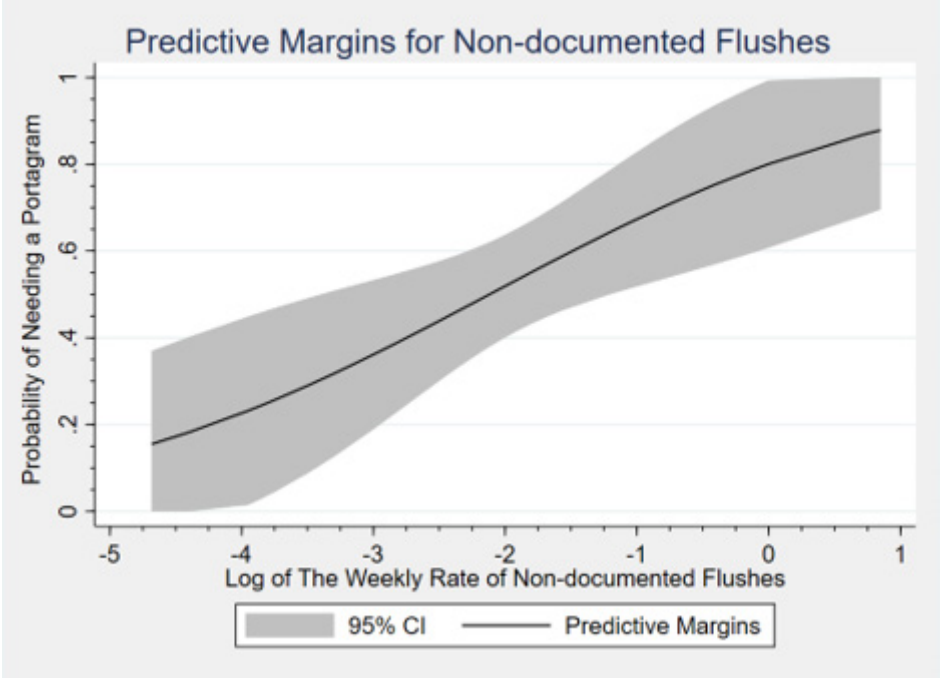

Figure 3 Predictive margins plot for probability of failure as a function of the log of the non-documented flushes weekly rate.

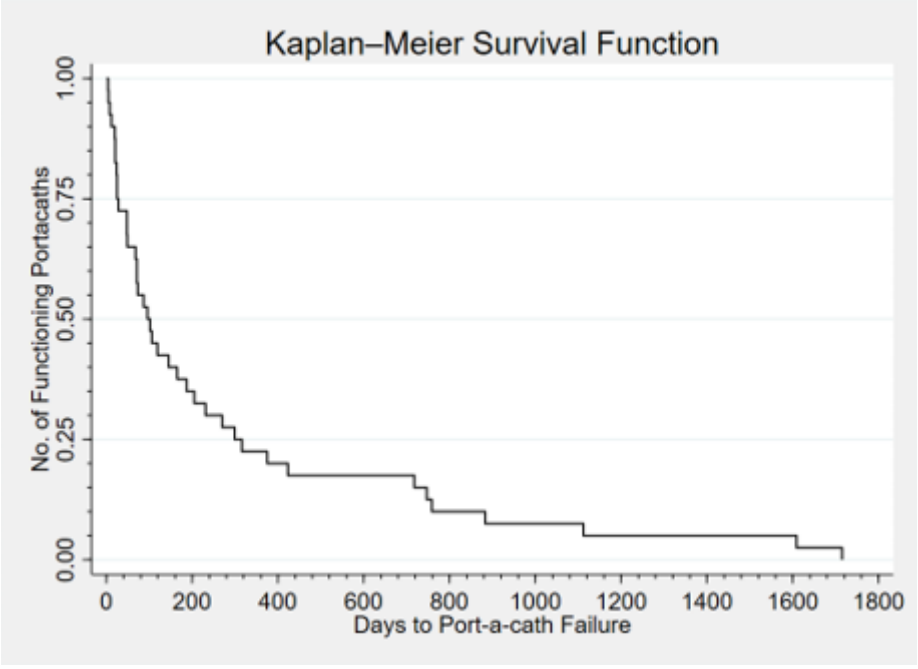

Figure 4 Kaplan-Meier survival function for TIVAD meeting the failure criteria. TIVAD, totally implanted vascular access devices.

and numerous other complications.[15–17] Further research is needed to replicate these results and identify modifiable risk factors that may result in suboptimal tip placement particularly in breast cancer patients.

The results for the second outcome suggest that more frequent flushing with heparinised saline and poor documentation of flushing were associated with a higher probability of TIVAD failure. The relationship between failure and both independent variables in the final model was found to be logarithmic in nature. These results are best interpreted in terms of the predictive margins which demonstrate that a 1% increase in the weekly rate of heparinised flushes and a 1% increase in the rate of non-documented flushes both increased the rate of TIVAD failure by 0.001 in this cohort. Current literature on the use of heparinised flushing demonstrates that there is no clear consensus on its efficacy over normal-saline flushing in preventing TIVAD occlusion.[18] A Cochrane review[19] in July 2022 found there to be little high-quality evidence to support the use of heparinised saline over normal saline for preventing occlusion. Results of this current study suggest that an increased frequency of heparinised saline flushes may be associated with an increased risk of TIVAD failure. Higher rates of poor documentation were also associated with TIVAD failure, the reasons for this association remain unclear by virtue of there being no documentation. The increased probability of failure associated with heparinised saline flushing contributes to an existing body of research that has failed to find heparinised saline to be a better alternative to normal saline in TIVAD locking. The increased probability of failure associated with poor documentation of flushes represents an area of clinical practice that can be easily improved, and which may provide benefit to patients with TIVAD.

Limitations

Some methodological limitations deserve comment. The portogram was a surrogate measure for TIVAD failure. The actual time of failure was not identified in the research and may influence the findings. Further, the nature of a design (case–control) has inherent limitations over experimental designs such as prospective randomised controlled designs. The single-centre experience with a small cohort may limit the external validity of the results.

CONCLUSION

This study investigated suboptimal TIVAD placement and subsequent failure of TIVAD. In this cohort, a statistically significant correlation was evident between breast cancer diagnosis and suboptimal tip placement. Further, increased flushing with heparinised saline and a lack of documentation were significantly associated with failure. Within the limits of the study design, a high failure rate of TIVAD was also detected.

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Contributors CM was responsible for data collection and review and overall content as the guarantor. GM was responsible for study design, write up and review. MT was responsible for statistical analysis and reporting. JE was responsible for write up and review. LN was responsible for assistance with study design, ethics and review. LR was responsible for data collection and initial statistical advice.

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Competing interests None declared.

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Patient consent for publication Not applicable.

Ethics approval Ethics approval was granted by the Human Research Ethics Committee at the author's organisation (HREC/LNR/2021/QTDD/75283).

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