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ORIGINAL ARTICLE

Musculoskeletal

A single-centre experience of 29 total ankle replacement in haemophiliac patients: Therapeutic management, factor consumption and cost

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Abstract

Introduction: In patients with haemophilia, repeated bleeding in large joints leads to chronic haemophilic arthropathy, a rare disease that can be managed surgically with ankle arthrodesis or with total ankle replacement (TAR). TAR has been reported to provide good surgical results in the medium/long-term and allow preservation of joint mobility but the medical therapeutic management of the patients has not been described.

Aim: To describe the medical therapeutic management of TAR.

Methods: All patients with haemophilia A/B, with haemophilic ankle arthropathy, and who underwent TAR between April 2006 and October 2019 were retrospectively included. Factor consumption, perioperative and early complications, volume of blood lost, and orthopaedic data were collected.

Results: A total of 25 patients underwent 29 TAR (mean age was 44.7 years [range: 26–65]). In the 17 patients with HA without history of anti-FVIII inhibitor, the mean \pm SD consumption the day of surgery was 116 ± 16 UI/kg when clotting factors were administered by continuous infusion, 106 ± 13 UI/kg when SHL factors were administered by bolus infusion, and 75 ± 22 UI/kg when EHL factors were administered by bolus infusion. During hospitalisation, the mean factor cost was €38,073 (83.7% of the total cost of surgery). Mean blood loss was significantly lower in patients treated with tranexamic acid (164 mL, range: 40–300) than in those not (300 mL, range: 70–800; $p = .01$). Six patients had haematoma. The 10-year survival free of any prosthesis removal/arthrodesis was estimated to be 92.2% (95% CI [83; 100]).

Conclusion: The medical therapeutic management of TAR is complex, carried out by a multidisciplinary team but effective in avoiding the occurrence of complications.

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KEYWORDS

ankle, arthropathy, haemophilia, total ankle replacement

1 | INTRODUCTION

Haemophilia is a haemorrhagic X-linked inherited disease that is due to a lack of Factor VIII for haemophilia A (HA) or Factor IX for haemophilia B (HB). The seriousness of the disease depends on the severity of the deficiency. In patients with mild or moderate disease, bleeding occurs with trauma; in those with severe disease, bleeding occurs spontaneously. Haemarthrosis is frequent in patients with haemophilia, and this mainly affects large joints such as the ankles, knees or elbows.^{1,2} Repeated bleeding leads to chronic haemophilic arthropathy, characterised by bone remodelling associated with pain.³ Haemophilic ankle arthropathy is a rare disease. It can be managed surgically with ankle arthrodesis or with total ankle replacement (TAR).^{4,5} Previously, ankle arthrodesis was the gold standard, but this type of procedure does not maintain the mobility of the joint.⁶ TAR has been reported to provide good surgical results in the medium to long-term and allow preservation of joint mobility^{7,8} and could increase quality of life,⁹ but the place of TAR remains debated¹⁰; furthermore, the medical therapeutic management of the patients (coagulation factors, use of tranexamic acid, other associated treatments) and results related to this management (factor consumption, associated costs) has not been described conversely to other joint replacement procedures.¹¹⁻¹³ The objective of the present study was therefore to describe the medical therapeutic management of TAR.

2 | MATERIALS AND METHODS

2.1 | Study design

In the present single-centre retrospective study, all patients with HA or HB, with haemophilic ankle arthropathy, and who underwent TAR between April 2006 and October 2019 were included. Patients aged under 18 years, protected by law (under guardianship or curatorship), or opposed to the use of their data were excluded. The patients were fully informed and provided written consent before the start of data collection. The study was approved by the local ethics committee (*Comité Scientifique et Éthique des Hospices Civils de Lyon*, n°20_248).

2.2 | Surgical management

Patients with haemophilia are followed by the haemophilia care centre of our institution. In cases of haemophilic arthropathy of the ankle, patients are referred to the senior foot and ankle surgeon. Only patients with severe pain resistant to analgesic drugs undergo TAR. Pre-operative assessment includes a physical examination (pain

location, ankle range of motion), the calculation of the American Orthopaedic Foot Ankle Society (AOFAS) ankle score (out of a total 100 points, with nine functional and clinical criteria),¹⁴ as well as weight-bearing ankle x-rays and a computed tomography (CT) scan. Patients receive intraoperative methylprednisolone (500 mg)¹⁵ and antibiotic prophylaxis (cefazolin 2 g or clindamycin 600 mg). The surgery is conducted in the supine position, with a tourniquet and a classic anterior approach. From 2006 to 2008, the AES prosthesis (Transystème SA, Nimes, France) was used, from 2009 to 2014 the Hintegra prosthesis (Newdeal SA, Lyon, France) was used, and since 2014 the Salto Talaris prosthesis (Tornier Wright, France) was used. At the end of the surgery, the surgical approach is closed with absorbable suture and drainage left in place for 2 days. At discharge from the surgical ward, patients are admitted to a rehabilitation centre to allow immediate rehabilitation to recover their range of motion and clinical monitoring, which plays an important role in the success of surgery.¹⁶ All are admitted to the same centre to facilitate the management of clotting factor concentrates. During rehabilitation patients are immobilised with non-weight-bearing posterior short-leg splint for 3 weeks, then a weight-bearing removable plastic boot for 3 weeks to stimulate skin healing and allow prosthetic integration. Patients are followed at 3 months, 6 months, 1 year, 2 years, and then every 5 years using the AOFAS ankle score, weight-bearing ankle x-rays, and a CT scan.

2.3 | Clotting factor management

In our haemophilia centre, a pharmacokinetic (PK) evaluation is performed before surgery to assess the patient's in vivo recovery. This also allows the verification of the absence of anti-FVIII/FIX antibodies. TAR is a surgery with a major risk of bleeding and therefore the blood factor concentration should be 80 IU/dL the first week and between 50 and 80 IU/dL the second and third postoperative week.¹⁷ A factor substitution protocol is provided by the haemophilia care centre and is adapted during hospital stay according to the clinical results and the patient's factor VIII or IX levels. The substitution protocol is continued for 3 weeks before administration of the usual prophylactic treatment. During rehabilitation, it is only adapted according to the clinical results. Until 2015 patients received clotting factors by continuous infusion (minipump) during hospital stay. From 2016, following the French commercialisation of two extended half-life factors (EHL; Elocta Swedish Orphan Biovitrum, Stockholm, Sweden, and Alprolix, Swedish Orphan Biovitrum), factors were administered by bolus infusion (BI). Patients were not to receive anticoagulant therapy, such as heparin or antiplatelet drugs, including during rehabilitation. After 2016 all patients received 1 g intravenous tranexamic acid intraoperatively as

many studies have shown the benefit of antifibrinolytics in reducing blood loss (BL) and transfusions after joint replacement.¹⁸ Patients wore support stockings after surgery for 3 weeks.

2.4 | Data extraction

The data collected from patient medical records (up to 2010 from paper files, and 2011 electronic patient records) were: demographic data (including age, body mass index [BMI], and type of haemophilia), medical history, length of hospital stay, factor consumption, perioperative and early complications (complications occurring within three months after surgery; occurrence of haemorrhagic complications [such as haematomas or haemarthrosis], infections, thromboembolic complications, fractures, development of anti-FVIII or anti-FIX inhibitors, delayed wound healing, and algodystrophy), volume of BL (reported during hospital stay by anaesthetists and nurses), blood haemoglobin level the day before the surgery and the third postoperative day, and orthopaedic data (revision surgery or not, AOFAS score, dorsiflexion, plantar flexion).

2.5 | Factor consumption and cost of TAR

One patient with severe HA treated with standard half-life (SHL) factors was excluded from the analysis of factor consumption because he was enrolled in a clinical trial and factor consumption was not known. Factor consumption was performed separately for the patient with mild HB because consumption is lower in such patients, and in the patient who had a previous history of anti-FVIII inhibitors because he received Feiba (Baxalta Innovations GmbH, Vienna, Austria). The total factor consumption corresponds to the 3 weeks of curative treatment. A cost analysis was conducted for the period including hospitalisation and rehabilitation, and considered costs of factors, prosthesis, and hospitalisation. For the rehabilitation period, we analysed the cost of factors administered in addition to the usual prophylactic treatment, that is to say, factors administered in the first 3 postoperative weeks. This was done using the official price of a unit of clotting factor in 2020 in France published by the health system, which was €0.648 for all factor VIII products. Then, the cost associated with only the factors for patients with HA and using either the published price (€0.648) or the price negotiated by our hospital (€0.648 for EHL factors, and €0.325 for SHL factors) was evaluated.

2.6 | Statistical analysis

Differences in quantitative variables between two independent groups were analysed using the Wilcoxon–Mann–Whitney test; differences between two paired groups were analysed using a signed Wilcoxon rank test. A *p*-value of $\leq .05$ was considered significant. The probability of survival was free of any prosthesis removal and free of any reoperation along with 95% confidence interval [95% CI] was estimated using

the Kaplan–Meier method. R (version 4.1.2, 2021, R Core Team) was used for all statistical analysis.

3 | RESULTS

3.1 | Characteristics of patients and surgeries

In total, 25 patients underwent 29 TAR, of which four bilaterally (all operated on by a senior surgeon, J.L.B.). All were male, the mean \pm SD age was 44.7 ± 12.1 years (range: 26–65) and the mean \pm SD BMI was 25.7 ± 3.9 kg/m² (range: 20–36). Diabetic patients were well controlled (HbA1c $\leq 6.5\%$) and atherosclerosis in one patient had no haemodynamic repercussions confirmed using ultrasound. There were 18 (72.0%) patients who had HA, one of whom had a previous history of anti-FVIII inhibitors (seven Bethesda Units, BU); this patient was treated with activated prothrombin complex concentrate (Feiba) and underwent one TAR. There were seven (28.0%) patients who had HB, one of whom had a mild HB and who underwent one TAR (Table 2). Of the surgeries performed, 17 (58.6%) were performed on the right ankle. There were 22 TAR (75.9%) in which SHL factors were used, six (20.7%) in which EHL factors were used, and one (3.4%) in which Feiba factors were used; there were seven surgeries performed before 2008, and 22 from the start of 2008 (Table 1). Among surgeries in which SHL factors were used, the mean \pm SD length of hospital stay for those performed from the start of 2008 (7.6 ± 1.5 days) was significantly lower than for those performed before 2008 (14.6 ± 1.5 days; *p* = .0002); among surgeries performed from the start of 2008, there was no significant difference in the mean \pm SD length of hospital stay between those in which SHL factors were used (7.6 ± 1.5 days) than those in which EHL factors were used (6.5 ± 0.8 days; *p* = .07). The mean follow-up was 5.8 years (range: 1–13.9); no patient was lost to follow-up.

3.2 | Clotting factor consumption and associated costs

The mean continuous infusion rate used during surgery was 3.95 IU/kg/h (range: 3.5–4.5) for patients with HA, and 5 IU/kg/h (range: 4–6) for those with HB. In the 17 patients with HA without a history of anti-FVIII inhibitor (who underwent 20 TAR), the mean \pm SD consumption on the day of surgery was 116 ± 16 UI/kg when clotting factors were administered by continuous infusion, 106 ± 13 UI/kg when SHL factors were administered by BI, and 75 ± 22 UI/kg when EHL factors were administered by BI. The mean \pm SD consumption in the first week was 504 ± 146 UI/kg when clotting factors were administered by continuous infusion, 416 ± 13 UI/kg when SHL factors were administered by BI, and 278 ± 41 UI/kg when EHL factors were administered by BI. In the six patients with moderate or severe HB (who underwent seven TAR), the mean \pm SD consumption the day of surgery was 193 ± 30 UI/kg when clotting factors were administered by continuous infusion, 162 ± 44 UI/kg when SHL factors were administered by BI, and 152 ± 31 UI/kg when EHL factors

TABLE 1 Surgical data.

	TAR n = 29
Arthroplasty with additional surgery, n (%)	18 (62.1)
Tibiotalar arthrolysis	2 (6.9)
Subtalar arthrodesis	9 (31.0)
In two steps	1 (3.4)
In one step	8 (27.6)
Talonavicular arthrodesis	1 (3.4)
Achilles tendon lengthening	9 (31.0)
Medial malleolar osteotomy	2 (6.9)
Ankle ligament plasty	5 (17.2)
Prosthesis, n (%)	
AES, Transysteme SA	7 (24.1)
Hintegra, Newdeal SA	6 (20.7)
SaltoTalaris (and/or XT), Tornier Wright	16 (55.2)
Mean surgery time (min)	133.1(80-250)
Tourniquet time (min)	96.9(66-144)

Abbreviation: TAR, Total ankle replacement.

were administered by BI. The mean \pm SD consumption in the first week was 696 ± 103 UI/kg when clotting factors were administered by continuous infusion, 580 ± 337 UI/kg when SHL factors were administered by BI, and 391 ± 0 UI/kg when EHL factors were administered by BI (Table 3). One patient with HA had a history of anti-FVIII inhibitors; consumption of Feiba in this patient was 190 IU/kg the day of surgery and 893 IU/kg the first week. Consumption of Mononine (CSL Behring, King of Prussia, PA, United States) on the day of surgery in a patient with mild HB was 132 and 342 UI/kg the first week.

During the first week of hospital stay, two patients (one with HA and continuous infusion, the other with HB and continuous infusion) required an increase in the daily dose of factor following a haemorrhagic complication. Eight patients had an increase in the daily factor dose because FVIII / FIX plasma activity was lower than 80 IU/dL, and 16 a decrease because it was higher than 80 IU/dL.

The mean total cost of surgery for HA and HB was €45,509; during hospitalisation, the mean factor cost was €38,073 (83.7% of the total cost of surgery), that of the prosthesis was €1,944 (4.3%), and that of hospitalisation was €5,492 (12.1%). The mean total cost of surgery for HA patients was €40,591, and factors accounted for 81.3% of this cost; the mean total cost of surgery for HB patients was €57,172, and factors accounted for 87.6% of this cost; the total cost for the HA patient with inhibitors was €134,931, and factors accounted for 90.3% of this. When published prices were used, in patients with HA the mean \pm SD daily cost of factors was €4,006 \pm 928 for those who received SHL factors by BI, and €2,153 \pm 344 for those who received EHL factors by BI; when negotiated prices were used, it was €2,009 \pm 465 for those who received SHL by BI, and 2,153 \pm 344 for those who received EHL fac-

tors by BI (Table 4). The mean \pm SD cost of factors during rehabilitation was €27,606 \pm 15,452 (43.3% of the total mean cost of factors).

3.3 | Short-term complications

The mean BL was 239 mL (range: 40–800) among all procedures. Mean BL were significantly lower in patients treated with tranexamic acid (164 mL, range: 40–300) than in those not (300 mL, range: 70–800; $p = .01$). The mean \pm SD decrease in haemoglobin level was significantly lower for patients treated with tranexamic acid (6.3 ± 9 g/L) than those not (12.4 ± 9 g/L; $p = .001$). There were 11 (37.9%) patients who experienced a short-term complication; six patients had haematoma that appeared between 1 day and 5 days after surgery; four had received one or more prophylactic doses of enoxaparin or ketoprofen within five postoperative days. No haemarthrosis episode, venous thrombosis, occurrence of anti-FVIII or anti-FIX inhibitor or algodystrophy was observed in these patients. Two patients suffered from a fracture of the medial malleolus; one patient did so after surgery and subsequently underwent osteosynthesis 4 days after surgery, and the other was detected during surgery (Table 5).

3.4 | Orthopaedic results and medium to long-term complications

The 10-year survival free of any prosthesis removal or arthrodesis was estimated to be 92.2% (95% CI [83;100]; Figure 1) and free of any reoperation to be 79.9% (95% CI [64;100]; Figure 2). One patient required surgical removal and five required revision of TAR (Table 5).

TABLE 2 Patient characteristics.

Patient	Surgery year	Prosthesis	Haemophilia	Form	Factor	Admini- stration	In vivo recovery	Continuous infusion rate during surgery (IU/kg/h)	Consumption the day of the surgery and first week (UI/kg)	Total factor consumption (UI/kg)	Length of stay (Days)	Blood loss (mL)	Tranexamic acid
1	2006	AES	B	Severe	Monomine	Continuous	1.1	5	763	1417	13	390	No
2	2006	AES	A	Severe	Helixate	Continuous	2.7	3.5	425	933	13	410	No
3	2007	AES	A	Severe	Kogenate	Continuous	2.9	3.5	603	1385	15	340	No
4	2007	AES	A	Severe	Helixate	Bolus	2.4	-	533	1265	15	300	No
5	2008	AES	B	Severe	Monomine	Continuous	1.0	6	915	1885	17	800	No
6	2008	AES	A	Severe ^a	Feiba	Bolus	NR	-	1083 ^a	2214 ^a	14	300	No
7	2008	AES	A	Severe	Advate	Continuous	1.9	4.5	988	1885	14	300	No
8	2010	HINTEGRA	B	Moderate	Betafact	Continuous	1.3	4	838	1634	7	300	No
9	2011	HINTEGRA	A	Moderate	Advate	Continuous	1.5	4.5	737	1460	7	270	No
10	2012	HINTEGRA	A	Severe	Advate	Continuous	1.9	4.5	636	1496	7	150	No
11	2012	HINTEGRA	A	Severe	Helixate	Continuous	2.8	3.5	511	1156	8	480	No
12	2014	HINTEGRA	A	Severe	Refacto	Continuous	2.3	4	561	1097	12	150	No
13	2015	TALARIS	A	Severe	Helixate	Continuous	2.6	3.5	507	1102	8	200	No
14	2015	HINTEGRA	A	Severe	Advate	Continuous	2.0	4.5	698	1342	6	70	No
15	2015	TALARIS	B	Severe	Betafact	Continuous	0.9	5	1038	1827	8	90	No
16	2016	TALARIS	A	Severe ^b	Kogenate	Bolus	2.5	-	.b	.b	8	250	No
17	2016	TALARISXT	A	Moderate	Advate	Continuous	2.6	4	685	1417	8	200	Yes
18	2016	TALARIS	B	Minor	Monomine	Bolus	NR	-	474	947	9	200	Yes
2*	2017	TALARISXT	A	Severe	Helixate	Continuous	2.7	3.5	477	808	8	200	Yes
19	2018	TALARIS	B	Severe	Benefix	Bolus	1.3	-	1012	1957	5	150	Yes
20	2018	TALARISXT	A	Severe	Advate	Bolus	2.1	-	538	1185	6	170	Yes
21	2018	TALARISXT	A	Severe	Elocta	Bolus	2.8	-	344	702	8	40	Yes
22	2018	TALARISXT	A	Moderate	Advate	Bolus	2.1	-	521	1193	7	100	Yes
23	2019	TALARISXT	B	Severe	Alprolix	Bolus	1.0	-	565	1282	7	100	Yes
24	2019	TALARIS	A	Severe	Elocta	Bolus	1.8	-	347	806	6	100	Yes
20 ^c	2019	TALARISXT	A	Severe	Nuwiq	Bolus	2.1	-	492	1185	8	300	Yes
23 ^c	2019	TALARISXT	B	Severe	Alprolix	Bolus	1.0	-	522	1043	6	140	Yes
21 ^c	2019	TALARISXT	A	Severe	Elocta	Bolus	2.8	-	329	597	6	235	Yes
25	2019	TALARIS	A	Severe	Elocta	Bolus	1.9	-	389	805	6	200	Yes

Note: Continuous: Continuous infusion; Bolus: Bolus infusion.

^a Patient with a history of anti-FVIII inhibitors treated with Feiba.

^b Patient enrolled in a clinical trial.

^c Patients who received a bilaterally TAR.

TABLE 3 Clotting factor consumption in patients with moderate or severe disease without history of inhibitors.

	Before tranexamic acid (<2016)			After tranexamic acid (≥2016)		
	BI and SHL ^c			BI and SHL ^c		
	Continuous infusion ^b	Mean consumption ± SD (IU/kg)	concentration (IU/dL) ^a	Continuous infusion ^b	Mean consumption ± SD (IU/kg)	concentration (IU/dL) ^a
Haemophilia A						
Number	9	1		2	3	4
Mean in vivo recovery	2.3	2.5		2.6	2.1	2.3
Day of surgery (day 0)	120 ± 15	122	133.5	102 ± 10	100 ± 8	75 ± 22
1st week (day 1-7)	510 ± 155	411	91.8	479 ± 137	417 ± 16	278 ± 41
2nd and 3rd week	688 ± 137	732	NR	532 ± 283	670 ± 23	375 ± 82
Total over 3 weeks	1317 ± 285	1265	NR	1113 ± 430	1187 ± 5	728 ± 100
Haemophilia B						
Number	4	0		0	1	2
Mean in vivo recovery	1.1	-		-	1.3	1.0
Day of surgery (day 0)	193 ± 30	-	120.0	-	193	152 ± 31
1st week (day 1-7)	696 ± 103	-	98.6	-	818	391 ± 0
2nd and 3rd week	802 ± 129	-	NR	-	946	619 ± 138
Total over 3 weeks	1691 ± 212	-	NR	-	1957	1162 ± 169

Abbreviations: BI, bolus infusion; EHL, extended half-life factors; SHL, short half-life factors.

^aBlood FVIII or FIX concentration (IU/dL).^bCoagulation factors administered by continuous infusion (Advate, Betafact, Helixate, Kogenate, Mononine, Refacto).^cCoagulation factors with SHL (Nuwiq, Advate, Helixate, Kogenate, Benefix, Mononine) administered by BI.^dCoagulation factors with EHL (Elocta, Alprolix) administered by BI.

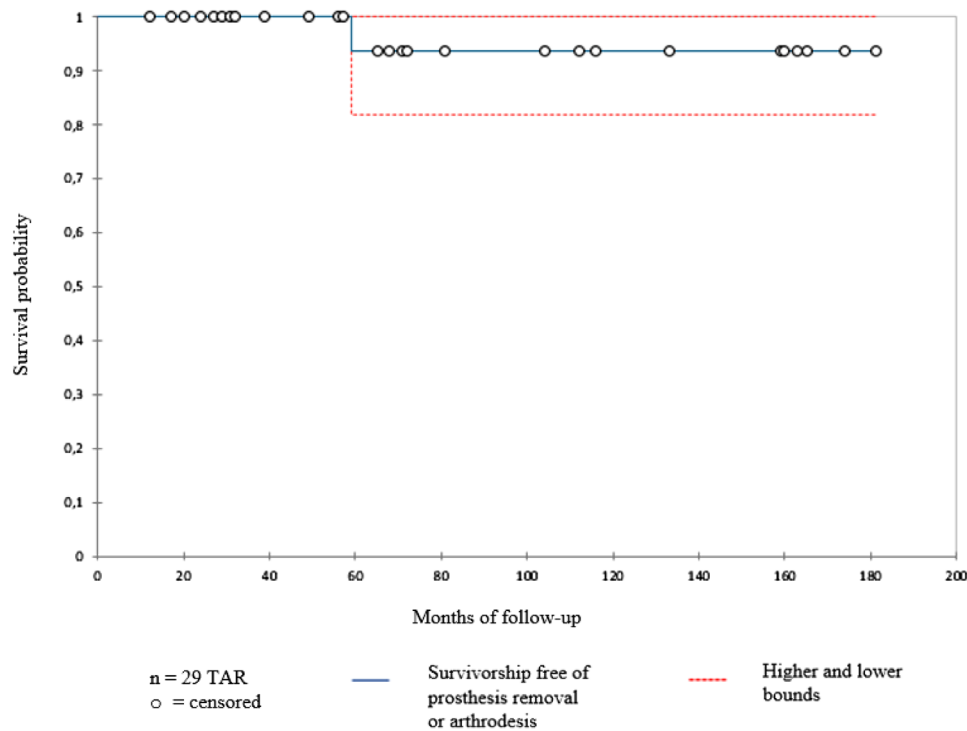


FIGURE 1 Kaplan-Meier analysis. Survivorship free of prosthesis removal or arthrodesis.

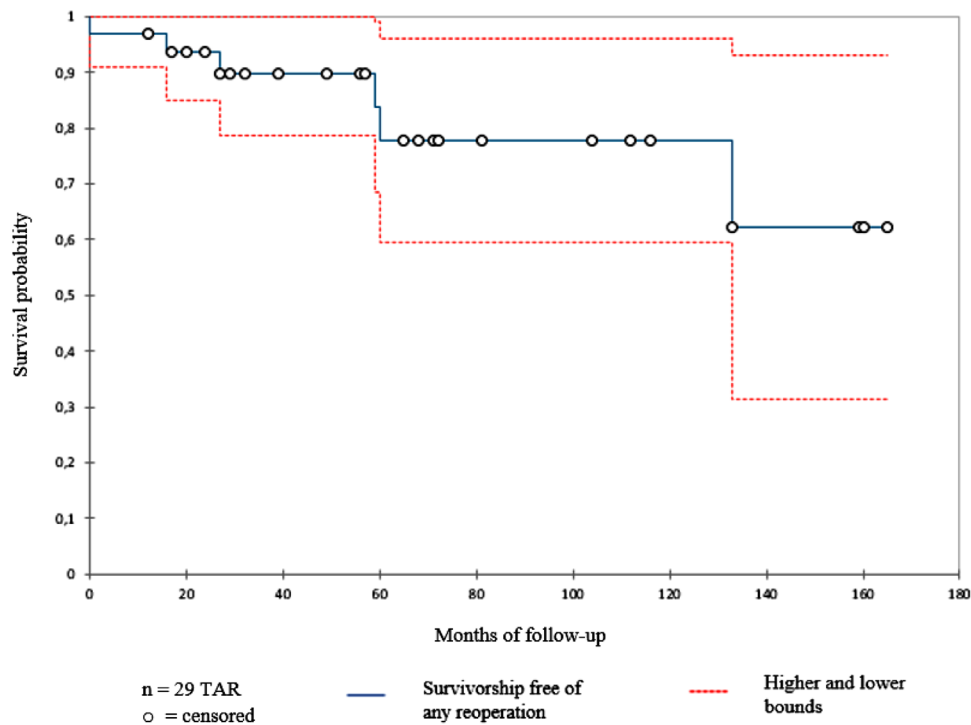


FIGURE 2 Kaplan-Meier analysis. Survivorship free of any reoperation.

The mean AOFAS score was 39.0 (range: 17–69) before surgery and was significantly improved 1 year after surgery (82.8; range: 68–98; $p < 10^{-5}$) and at the last follow-up (83.0; range: 71–98; $p < 10^{-4}$). Dorsiflexion was significantly improved; increasing from a mean \pm SD

$-2.3 \pm 8.9^\circ$ preoperatively to $9.6 \pm 4.7^\circ$ at the last follow-up ($p < .01$). No significant difference was found between the mean \pm SD pre- ($29.4 \pm 8.4^\circ$) and post-operative plantar flexion ($28.4 \pm 7.5^\circ$ at the last follow-up).

TABLE 5 Short and long-term complications.

Case	Patient	Prosthesis	Short-term complications	Long-term complications
1	1	AES	No	Re-operation at 60 months for Achilles tendon lengthening
2	2	AES	No	Re-operation at 133 months for geode cementation and extensive arthrolysis
4	4	AES	Haematoma Delayed wound healing	Re-operation at 27 months for osteophytes of the medial malleolus
5	5	AES	Delayed wound healing	No
7	7	AES	Important haematoma	Removal surgery at 59 months due to aseptic loosening on large geodes. Tibial-talar arthrodesis was performed
9	9	HINTEGRA	Haematoma	No
10	10	HINTEGRA	Haematoma	No
13	13	TALARIS	Delayed wound healing	No
15	15	TALARIS	Important haematoma Delayed wound healing	No
16	16	TALARIS	Delayed wound healing	No
23	22	TALARIS XT	Fracture of the malleolus, underwent osteosynthesis four days after surgery	No
27	23	TALARIS XT	Haematoma progressing to surgical site infection 22 days after surgery	Re-operation was necessary 13 months later because of infection
28	21	TALARIS XT	Fracture of the malleolus	No

has since been withdrawn from the market in 2009 because it caused too many surgical revisions.²⁵ Interestingly, the results of the present study seem to indicate a better estimated implant survival than in previous studies of TAR; for instance 85% at 10 years reported by Eckers et al.⁸ However, BL appears to be lower in the present study for TAR than that reported for total hip replacement or total knee replacement (this has not been reported for TAR); for instance Zhai et al. reported mean BL of 1350 mL following total hip replacement and 625 mL following total knee replacement.²⁶ In our hospital, BL seems equivalent to healthy patients. However, the data concerning BL lacks precision because this is a retrospective study and the measurement of these BL was operator-dependent, which is a limitation. Furthermore, although factor consumption data was available for all-but-one patient (who was included in a clinical trial and whose data could not be retrieved), it is of note that the single-centre design limited the number of patients included. Moreover, the long study period with changes to the protocol led to comparisons being made in small subgroups with very small numbers. Despite this limitations, this study provides new data in patients with haemophilia who underwent TAR with a medium to long follow-up. These data were obtained in a single-centre, which offers the advantage of having homogeneous and reproducible data from a single multidisciplinary team including haemophilia comprehensive care centre, orthopaedic surgeons and pharmacists because they all use a homogeneous management protocol.

5 | CONCLUSION

The medical therapeutic management of TAR is complex, carried out by a multidisciplinary team but effective in avoiding the occurrence of complications. Another multicentre clinical study could confirm the impact of this multidisciplinary team on survival, clinical and functional outcomes.

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CONFLICT OF INTEREST STATEMENT

The authors stated that they had no interests which might be perceived as posing a conflict or bias.

ETHICS STATEMENT

The study was approved by the local ethics committee (Comité Scientifique et Éthique des Hospices Civils de Lyon, n° 20_248).

DATA AVAILABILITY STATEMENT

Data are available on reasonable request from the authors.

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