RANDOMISED CONTROLLED TRIAL

Editor's Choice – A Cost Effectiveness Analysis of Outpatient *versus* Inpatient Hospitalisation for Lower Extremity Arterial Disease Endovascular Revascularisation in France: A Randomised Controlled Trial

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WHAT THIS PAPER ADDS

AMBUVASC was the first cost effectiveness analysis associated with a prospective randomised controlled trial in France that compared outpatient *vs.* inpatient hospitalisation for the endovascular repair of lower extremity arterial disease (LEAD). From a societal perspective, considering a one month time horizon, outpatient hospitalisation was not cost effective compared with inpatient hospitalisation for a €50 000 per quality adjusted life year (QALY) threshold (the incremental cost effectiveness ratio was €67 741 per QALY). This result was mainly explained by the higher number of re-admissions in the outpatient arm. More data are required to support the cost effectiveness for LEAD endovascular revascularisation.

Objective: The AMBUVASC trial evaluated the cost effectiveness of outpatient *vs.* inpatient hospitalisation for endovascular repair of lower extremity arterial disease (LEAD).

Methods: AMBUVASC was a national multicentre, prospective, randomised controlled trial conducted in nine public and two private French centres. The primary endpoint was the incremental cost effectiveness ratio (ICER), defined by cost per quality adjusted life year (QALY). Analysis was conducted from a societal perspective, excluding indirect costs, and considering a one month time horizon.

Results: From 16 February 2016 to 29 May 2017, 160 patients were randomised (80 per group). A modified intention to treat analysis was performed with 153 patients (outpatient hospitalisation: $n = 76$; inpatient hospitalisation: $n = 77$). The patients mainly presented intermittent claudication (outpatient arm: 97%; inpatient arm: 92%). Rates of peri-operative complications were 20% (15 events) and 18% (14 events) for the outpatient and inpatient arms respectively ($p = .81$). Overall costs (difference: €187.83; 95% confidence interval [CI] −275.68—651.34) and QALYs (difference: 0.00277; 95% CI −0.00237 — 0.00791) were higher for outpatients due to more re-admissions than the inpatient arm. The mean ICER was €67 741 per QALY gained for the base case analysis with missing data imputed using multiple imputation by predictive mean matching. The outpatient procedure was not cost effective for a willingness to pay of €50 000 per QALY and the probability of being cost effective was only 59% for a €100 000/QALY threshold.

Conclusion: Outpatient hospitalisation is not cost effective compared with inpatient hospitalisation for endovascular repair of patients with claudication at a €50 000/QALY threshold.

Keywords: Conventional hospitalisation, Cost effectiveness, Endovascular, Outpatient, Peripheral arterial occlusive disease
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INTRODUCTION

The worldwide prevalence of peripheral arterial occlusive disease (PAOD) is rising, in connection with factors like population ageing and greater prevalence of diabetes and renal failure.[1,2] Vascular interventional specialists have to respond to a greater need for hospitalised care at a time of ever growing pressure on the financing of healthcare expenditures.[3] Moreover, patients are increasingly well informed about existing solutions that are safe and effective, and they seek prompt recovery. Specialists should therefore find ways to minimise use of resources without compromising the quality, safety, and effectiveness of patient care.

Endovascular repair for lower extremity arterial disease has become widespread over the past decades due to continuous improvements in technological and minimally invasive approaches.[4] It has the potential to meet the stated needs — controlled hospital expense and quick patient recovery — through same day hospital discharges.[5]

Many countries are encouraging recourse to ambulatory care.[6] In the United States, there is a major thrust to move patients out of hospital rooms and into day hospitals and physicians' offices for endovascular interventions to treat lower limb PAOD.[7] Yet, in spite of this trend, there is a lack of evidence about the cost effectiveness of ambulatory endovascular procedures for lower extremity arterial disease (LEAD). Recently, a single centre randomised clinical trial including 19 patients assessed the safety of same day discharge *vs.* overnight stays following peripheral arterial interventions but Islam *et al.* did not evaluate the costs of the procedure.[8]

The goal of the AMBUVASC randomised controlled trial was to assess the cost effectiveness of outpatient compared with inpatient hospitalisation for endovascular repair for LEAD.

MATERIALS AND METHODS

Study design

AMBUVASC was a national multicentre, prospective, open label randomised controlled trial conducted in nine public and two private French centres of vascular and endovascular surgery. Each site was highly experienced with outpatient and inpatient endovascular treatment for PAOD. Patients were included and randomly assigned in a 1:1 ratio to either outpatient or inpatient hospitalisation. Web based block randomisation was employed. Stratification by investigational site was used to ensure proportional assignment. The main objective was to perform a cost effectiveness analysis, calculating incremental cost per quality adjusted life year (QALY) for outpatient *vs.* inpatient endovascular LEAD interventions. The trial was conducted in accordance with International Council for Harmonisation (E6), French Good Clinical Practice guidelines, and relevant regulations. It was approved by a French ethics committee (IDRCB 2015-A01077-42, ref. 18/15, 9 September 2015) (Clinical Trial number: NCT02581150; 20 October 2015).

Patients

The sample size was determined according to the net benefit criterion, that is the difference in monetary terms between the expected difference in costs and in QALYs, the latter being monetised by multiplying QALYs by the willingness to pay a QALY.[9] Based on a retrospective analysis of 100 patients in the study's leading hospital, it was assumed that outpatient surgery might save costs (−884 euros) and slightly improve quality of life (+0.0017 QALYs). For a conservative willingness to pay €22 400 and various assumptions regarding the remaining technical parameters as well as an assumption of 10% of patients lost during follow up, the required sample size varied between 68 and 80 patients per arm (assuming a type I error of 5% and a power of 80%).[10]

Patients were eligible for enrolment if they had a history of symptomatic LEAD with intermittent claudication (Rutherford categories 1—3), requiring diagnostic catheterisation or endovascular repair compatible with a size 5—7 French sheath. They had to be in American Society of Anesthesiologists Physical Status categories I to III (stabilised) and able to walk. Finally, patients had to be registered in the French national health insurance system. Patients with haemostasis disorders, with acute ischaemia, for whom outpatient hospitalisation was not an option per Société Française d'Anesthésie et de Réanimation guidelines,[11] for whom endovascular treatment was contraindicated, or who had previously participated in the AMBUVASC trial were excluded. Patients for whom interventions required a sheath larger than 7 French or radial, brachial, or antegrade femoral approaches were also excluded. All patients provided written informed consent.

Hospitalisation and procedures

Patients randomly assigned to outpatient hospitalisation were hospitalised in the morning of the day of the surgical endovascular intervention (D0: Day 0), and they were discharged the same day after at least 4 h of post-operative follow up and a medical examination. Patients randomly assigned to inpatient hospitalisation were hospitalised the day before or in the morning of the day of intervention, and they were discharged the day following the intervention after a medical examination. For both arms, index procedures, and re-interventions were left to the operators' discretion and did not differ between arms but for the use of vascular closure devices (VCDs). Indeed, use of VCDs was only mandatory for the outpatient arm. One month after their procedures, patients had medical appointments during which data on quality of life, consumption of health resources, complications, and symptoms were collected.

Outcomes

The primary endpoint was the incremental cost effectiveness ratio (ICER), which represents the extra cost for each QALY gained when comparing outpatient with inpatient hospitalisation. The analysis was conducted from a societal

perspective using a one month time horizon. The purpose was to capture differences in costs and QALYs due to the type of procedure, that is inpatient or outpatient hospitalisation, and not differences attributable to the natural course of the disease whatever the type of hospitalisation. This is the reason a short time horizon was selected. As per French guidelines for the economic evaluation of healthcare programmes, only direct costs were considered.[12] Costs were estimated by[1] counting prospectively the type and quantity of resources used in and outside the hospital,[2] determining a unit monetary cost for each resource consumed,[3] multiplying the unit costs by the quantities of the corresponding resources, and[4] adding up the costs thus estimated. Regarding the first step, the duration of the initial hospitalisation stay was collected and a microcosting approach was used to precisely estimate the hospital's production cost for the intervention. This consisted of counting the number of implantable medical devices used and the time spent by each professional in the operating and recovery rooms. Using patients' diaries and the French national medical information system, the resources used were collected during the one month follow up period: pain medication, consultations (with general practitioner or specialists), nurses and emergency visits, additional hospitalisations, laboratory analyses, radiological examinations, and domestic help, whether paid or from informal caregivers. Unit costs for resources used were determined as follows. Healthcare professionals' mean gross wages (in the leading hospital) and the prices charged to hospitals for medical devices were used to value the resources collected by microcosting during the intervention. "Hotel" costs (hospital costs apart those related to the intervention) for initial hospital stays were estimated using the annual French national cost study (Étude Nationale des Coûts). This study estimates average hospital production costs per Diagnosis Related Group (DRG) from the analytical accounting systems of two national samples of public and private hospitals.[13] From these average costs those related to the intervention (estimated by microcosting) were subtracted and the national mean length of stay was employed to determine daily hospital hotel costs for each patient's DRG. For follow up costs, including those for additional hospitalisations, unit costs were determined by the French National Health Insurance tariffs in 2017. The professionals' wages were employed as proxies for the opportunity costs of domestic help whether provided by professional or informal caregivers. Total costs were obtained by multiplying the quantity for each resource by the corresponding unit cost and by summing hotel costs, intervention costs, and follow up costs (see Table 4). All costs were valued in 2017 euros. QALYs were estimated from patients' answers to the EuroQol EQ-5D-3L quality of life questionnaire at the time of inclusion, two days after the intervention, and one month after the intervention.[14] The utility values of the corresponding health states were obtained from the preference weights of a representative sample of the French population.[15] The number of QALYs was calculated by applying an area under the curve method.[16]

A procedure was considered successful if a technical success was obtained for each treated lesion. The technical success was defined as achievement of a final residual diameter stenosis of $< 30\%$ on the procedural completion angiogram. The major adverse events at 30 days included death from any cause, stroke, and myocardial infarction, major amputations (transfemoral and transtibial). Stroke was defined as a sudden, focal neurological deficit resulting from a cerebrovascular cause, resulting in death or lasting longer than 24 h. Myocardial infarction was defined as presumed ischaemic symptoms (chest pain, new ST segment elevation of greater than 1 mm in two or more contiguous leads and troponin level higher than two times the upper limit of the normal). Peri-operative vascular complications related to the index procedure were divided into major and minor. Major vascular complications were re-intervention; bleeding requiring subsequent manual compression, vascular surgical or interventional treatment; haemoglobin decrease by 2 g/dL; pseudo-aneurysm formation; access site infection; acute limb ischaemia related to embolisation, dissection, or thrombosis. The clinical and haemodynamic improvement were assessed by the Rutherford Baker categories and the resting ankle brachial index (ABI) measurement.

Statistical and cost effectiveness analysis

The ICER was calculated from a societal perspective. The base case results come from a modified intention to treat analysis with multiple imputations for missing data. Missing data for costs are reported (see Table 4). There were 9% and 10% missing EQ-5D measures at day 2 and day 30 respectively. Data were assumed to be missing at random and fitted chained imputation models for costs and EQ-5D scores using predictive mean matching.[17] Twenty imputed datasets were generated. The imputation models used cost items, QALYs, age, body mass index (BMI), hospital status (public or private), and the Rutherford score at baseline. The probability that outpatient hospitalisation would be cost effective was assessed across a range of societal willingness to pay thresholds using a seemingly unrelated regression analysis (SUR). SUR consists in the estimation of a system of joint regression equations, one for costs and one for QALYs, which allows one to consider the correlation between costs and QALYs. A further advantage of this method is that it is generally robust to skewness in the data.[18] In the system estimated, costs were regressed on the study's arm and QALYs were regressed on the study's arm and on the EQ-5D baseline score to adjust for potential imbalance between arms. The coefficients corresponding to the study's arm in the two (jointly estimated) models provide the respective mean differences between costs and QALYs that serve to estimate the incremental cost effectiveness ratio. Several sensitivity analyses were also performed: first, the consequences of uncertainty in estimates of hotel costs were explored, as they represent the main source of potential savings when replacing inpatient with outpatient hospitalisation. Second, the assumption of data

missing at random were considered, reperforming analyses for various deterministic patterns of missing data.[19] Third, the results of the base case analysis were compared with those obtained from the complete case sample. Analyses were performed with Stata software, version 15 (StataCorp LLC, College Station, TX, USA).

RESULTS

From 16 February 2016 to 29 May 2017, 160 patients were enrolled and 80 patients were assigned to each arm. Among outpatients, eight were not hospitalised as planned. Three of them were deemed ineligible for outpatient hospitalisation by the anaesthesiologist and required inpatient hospitalisation, and one patient refused to be an outpatient. These four remained in the outpatient arm for the purpose of modified intent to treat analysis even though they were to undergo inpatient hospitalisation. Three other patients in the outpatient arm were not eligible to participate due to exclusion criteria for endovascular interventions, and the intervention for another patient was postponed to a date outside the study's time frame: these four were excluded from analysis. In the inpatient arm, one patient refused inpatient hospitalisation. Though due to receive outpatient hospitalisation instead, this patient remained in the inpatient arm for the purposes of analysis. For two patients, interventions were postponed to dates outside the study time frame, and one patient withdrew consent: these three patients were excluded from the analysis. Consequently, modified intention to treat analysis was performed for 76 patients in the outpatient arm and 77 patients in the inpatient arm. Characteristics of patients in the modified intention to treat population were well balanced between arms (Table 1). Symptomatology justifying treatment was intermittent claudication of the lower limbs (outpatient arm: 97%; inpatient arm: 92%), and the American Society of Anesthesiology Physical Status categories, mainly between two and three (outpatient arm: 96%; inpatient arm: 94%). Three per cent and 8% of patients with Rutherford category 4 were included in the outpatient and inpatient group respectively.

Procedural characteristics and target lesions at baseline are described in Table 2. Overall, the most commonly treated lesions in both arms were aorto-iliac, followed by femoropopliteal. Arms differed (outpatient arm; inpatient arm; p value) in rates of stenting in treated limbs (96%; 86%; $p = .030$), recourse to manual compression (30%; 70%; $p < .001$), and use of VCDs (97%; 62%; $p < .001$).

Peri-operative events are indicated in Table 3. During the peri-operative period, there was one death at 16 days in the outpatient arm, but it was not related to the intervention or PAOD. In the outpatient arm, among the 76 patients analysed, 68 (89%) were discharged on the same day. The remaining patients ($n = 8$) remained hospitalised for one or more nights because they requested this ($n = 2$) or due to adverse events ($n = 6$). In the inpatient arm, among the 77 analysed patients, 55 patients (71%) were hospitalised two nights; 20 patients (26%), one night; one patient (1%), four nights; and one patient (1%) was not hospitalised overnight. Peri-operative major vascular complications were suffered by eight patients in the outpatient arm and five patients in the inpatient arm. These complications were mainly observed intra-operatively and within the first hours following the intervention. There were three re-admissions (two patients) in the peri-operative period in the outpatient arm. No one in the inpatient arm was re-admitted. There were five peri-operative re-interventions (four patients) in the outpatient arm and one in the inpatient arm (5% and 1% respectively; $p = .21$). Two of the outpatient

Table 1. Baseline demographic and clinical characteristics of 153 patients with lower extremity arterial disease included in the intention to treat population

	Outpatient arm ($n = 76$)	Inpatient arm ($n = 77$)
Mean age ± SD − y	64 ± 10	62 ± 11
Median age (IQR) − y	65 (13)	62 (13)
Male sex	67 (88)	70 (91)
Hypertension	53 (70)	44 (57)
Hyperlipidaemia	47 (62)	46 (60)
Diabetes mellitus	19 (25)	23 (30)
Smoker	34 (45)	39 (50)
Coronary disease	19 (25)	15 (19)
Renal insufficiency	2 (3)	3 (4)
On dialysis	0 (0)	0 (0)
ASA I/II/III	3 (4)/41 (54) /32 (42)	5 (6)/42 (55) /30 (39)
Claudication	73 (97)	71 (92)

Data are presented as n (%) unless stated otherwise. SD = standard deviation; IQR = interquartile range; ASA I/II/III = American Society of Anesthesiology Physical Status categories; y = year.

Table 2. Procedural characteristics and target lesions at baseline in 153 patients treated by endovascular repair for lower extremity arterial disease

	Outpatient arm ($n = 76$)	Inpatient arm ($n = 77$)	p value
Anaesthesia			.67
Local + sedation	42 (55)	37 (48)	
Locoregional	5 (7)	6 (8)	
General	29 (38)	34 (44)	
Diagnostic catheterisation	13 (17)	13 (17)	.97
Angioplasty	7 (9)	13 (17)	.16
Stenting	73 (96)	66 (86)	.030
Treated iliac lesions	48 (62)	50 (64)	.47
Treated femoropopliteal lesions	42 (53)	44 (55)	.92
Manual compression	23 (31)	54 (70)	<.001
Use of VCD	74 (97)	48 (62)	<.001
Compression dressing	27 (36)	51 (67)	<.001
Technical success	73 (96)	76 (99)	.37
Intervention duration − min	49 (45) ± 26	47 (45) ± 28	.60

Data are presented as n (%) or mean (median) ± standard deviation. VCD = vascular closure device.

Table 3. Peri-operative events in 153 patients treated by endovascular repair for lower extremity arterial disease

	Outpatient arm (n = 76)	Inpatient arm (n = 77)	p value
Peri-operative death	1 (1)	0 (0)	
Hospitalisation duration			
Same day discharge	68 (89)	1 (1)	<.001
1 night	2 (3)	20 (26)	
2 nights	4 (5)	55 (71)	
≥3 nights	2 (2)	1 (1)	
Peri-operative complications	15 (20)	14 (18)	.81
Peri-operative re-admissions	2 (3)	0	.25
Peri-operative re-interventions	4 (5)	1 (1)	.21

Data are presented as n (%).

arm re-interventions were open conversions due to an arterial dissection and an arterial embolism and were performed within the first few hours following the index intervention. The remaining three re-interventions were performed 15 days after patient discharge. The sole inpatient arm re-intervention was performed just before patient discharge. Moreover the rate of peri-operative complications, re-interventions, or re-hospitalisation was not correlated with the type of procedure (diagnostic angiography, interventional angiography) ($p = .30$).

In general, symptoms, expressed as Rutherford categories, had improved for both arms at one month (by −3,−2, or −1 in 47% of the outpatient arm and 44% of the inpatient arm; $p = .84$). The resting ankle brachial index was significantly improved at one month compared with baseline in both groups (for outpatient arm, 0.72 ± 0.19 at D0 *vs.* 0.93 ± 0.18 at one month [M1]; for inpatient arm, 0.72 ± 0.19 at D0 *vs.* 0.98 ± 0.20 at M1, $p < .001$), there being no significant difference between the groups at M1 ($p = .39$).

Fig. 1 plots the mean EQ-5D scores over time. In both arms, health related quality of life scores increased significatively between baseline and M1. The corresponding QALYs (the areas under the curves in Fig. 1) are 0.06820 for the outpatient arm and 0.06558 for the inpatient arm (see Table 5), yielding a difference ($= QALY_{outpatient} - QALY_{inpatient}$) of 0.00277 (95% confidence interval [CI] −0.00237 − 0.00791) when adjusting for baseline EQ-5D.

Table 4 shows estimated costs. Costs associated with the intervention and the initial hospital stay are the greatest contributors. Microcosting estimates of intervention production costs are higher for the outpatient than inpatient arm (€1789 and €1642 respectively). This difference is mostly due to the mean cost of VCDs (outpatient arm: €167, median: 142; interquartile range [IQR]: 130, 68); inpatient arm: €98, median: 130; IQR: 0, 138; details not provided). Mean cost of vascular endoprostheses did not differ between arms (outpatient arm: €1305, median: 830, IQR: 775, 1550; inpatient arm: €1252, median: 1550, IQR: 775, 1550; details not provided). In contrast, mean hotel costs for initial hospital stays were greater in the inpatient arm (€1698) than in the outpatient arm (€1 481). All follow up costs for the inpatient arm exceeded those for the outpatient arm, with the exception of costs of domestic help and re-admission. Mean re-admission costs are conspicuously higher for the outpatient arm (€302 *vs.* €0, respectively) because there were no inpatient arm re-admissions. Owing to higher intervention and rehospitalisation costs for the outpatient arm, the total mean cost per patient was higher for that group than for the inpatient arm, yielding a difference of €187 (95% CI −275.68−651.34) (Table 5).

The mean ICER was €67 741 per QALY gained for the base case analysis (Table 5). To account for statistical uncertainty surrounding this estimation, probabilities of outpatient interventions being cost effective when compared with inpatient interventions were calculated. Fig. 2 plots these probabilities for various willingness to pay values. The bold curve (base case analysis) in Fig. 2 shows that the outpatient procedure is unlikely to be cost effective since the probability exceeds 50% only if the willingness to pay for an additional QALY is greater than €68 000, and it only reaches 59% when willingness to pay is €100 000. To assess the robustness of the results, various sensitivity analyses were conducted. First, the ICER was calculated for 10% lower and 10% higher hotel costs in the outpatient arm, to explore the uncertainty around top down estimates based on average charges per DRG. A 10% decrease makes the outpatient procedure cost effective for a willingness to pay as low as €20 000/QALY (red curve in Fig. 2), while, as expected, a 10% increase did not affect the results (green curve in Fig. 2). Second, the possibility of data not missing was tested at random by replacing imputed values with consistently lower or higher QALYs and costs in both arms. With this hypothesis, the

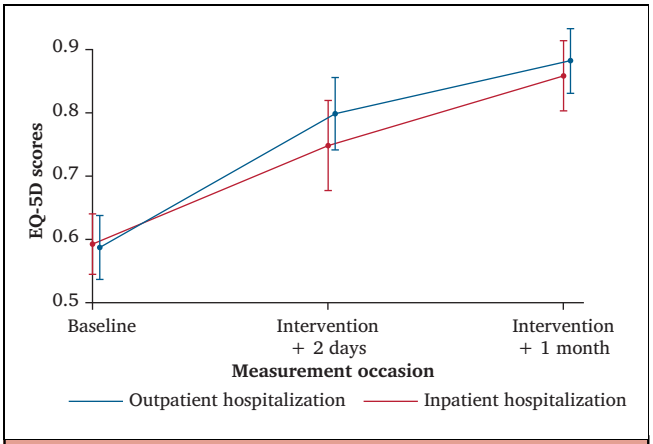

Figure 1. Health related quality of life scores (EQ-5D) over time for 76 patients in outpatient and 77 patients in inpatient arm in complete case analysis with imputed data endovascular repair for lower extremity arterial disease. The data were missing for 0%, 11.69%, and 10.39% for the inpatient arm and for 1.32%, 6.58%, and 10.53% in the outpatient arm at baseline, two days after intervention, and one month after intervention, respectively.

Table 4. Cost estimates per item and per patient (base case analysis) in 153 patients treated by endovascular repair for lower extremity arterial disease

	Outpatient arm (n = 76)		Inpatient arm (n = 77)	
	Mean	Median (IQR)	Mean	Median (IQR)
Initial hospital stay				
Intervention costs[*]	1 789.73	1 509.79 (1 187.19, 2 111.87)	1 642.07	1 736.62 (1 122.57, 1 989.36)
Missing — %	14.29		13.16	
Hotel costs[†]	1 481.39	1 242.02 (1 242.02, 1 752.39)	1 698.79	1 767.74 (1 460.21, 1 767.74)
Missing — %	0		0	
Follow up				
Consultations, GP	10.53	0 (0, 25)	16.95	5 (0, 25)
Missing — %	6.49		6.58	
Consultations, specialist	14.19	0 (0, 30)	18.19	30 (0, 30)
Missing — %	6.49		5.26	
Pain medication	2.62	0 (0, 1.85)	3.59	0 (0, 4.21)
Missing — %	9.09		6.58	
Radiological exams	60.79	69.93 (66.43, 69.93)	85.14	69.93 (69.93, 69.93)
Missing — %	6.49		3.95	
Laboratory analyses	2.42	0 (0, 4.86)	3.09	0 (0, 4.86)
Missing — %	6.49		3.95	
Nurses' visits	22.23	0 (0, 0)	35.63	0 (0, 0)
Missing — %	6.49		3.95	
Domestic help	21.87	0 (0, 0)	16.20	0 (0, 0)
Missing — %	6.49		6.58	
Emergency visits	0.33	0 (0, 0)	1.46	0 (0, 0)
Missing — %	6.49		3.95	
Hospitalisations	302.83	0 (0, 0)	0	0 (0, 0)
Missing — %	6.49		3.95	

Data are in 2017 euros. GP = general physician; IQR = interquartile range.
* Intervention costs were determined through microcosting.
† Authors' estimations using the annual French national cost study (Étude Nationale des Coûts) for hospital charges.

Table 5. Mean costs (2017 euros), mean QALYs, and incremental cost effectiveness ratio (ICER) for 77 patients in the inpatient arm and 76 patients in the outpatient arm treated by endovascular repair for lower extremity arterial disease

	Mean QALYs (95% CI)	Mean costs (95% CI)
Inpatient hospitalisation	0.065 (0.064−0.066)	3 521.12 (3 304.03−3 738.21)
Outpatient hospitalisation	0.068 (0.066−0.069)	3 708.95 (3 285.06−4 132.84)
Difference[*]	0.002 (−0.002−0.007)	187.83 (−275.68−651.34)
ICER	€67 741 per QALY gained	

CI = confidence interval; ICER = incremental cost effectiveness ratio; QALY = quality adjusted life year.
* Difference in QALYs adjusted for baseline difference in EQ-5D utility scores.

threshold corresponding to a cost effectiveness of outpatient hospitalisation (when probability is 50%) is changed, but it never drops below €60 000/QALY: the orange curve in Fig. 2 is an example missing not at random scenario. Finally, all analyses were performed for the complete case sample which is made of 52 patients in each arm (inpatient and outpatient arms) by removing those individuals for which at least one information was missing. In this case, the outpatient procedure is very likely to be cost effective, even at a low willingness to pay. The reason for such an apparently contradictory finding is that re-admitted outpatient arm patients who had above average costs were also missing data and were consequently excluded from the complete case sample. Thus, re-admission largely explains why the outpatient procedure is costlier and not cost effective at a willingness to pay of €50 000/QALY.

DISCUSSION

AMBUVASC was the first cost effectiveness analysis associated with a randomised controlled trial that compared outpatient and inpatient hospitalisation for endovascular repair of LEAD.

A threshold value for a QALY has yet to be recommended in France. To facilitate interpretation, a value of €50 000/QALY was arbitrarily chosen, which is higher than the

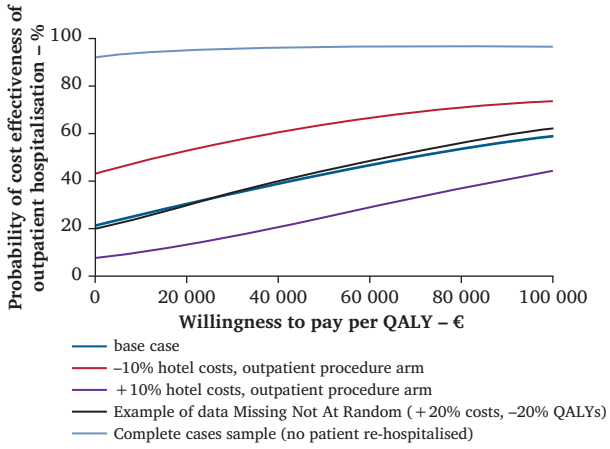

Figure 2. Cost effectiveness acceptability curves for base case analysis and for sensitivity analysis scenarios in endovascular repair for lower extremity arterial disease. QALY = quality adjusted life year.

thresholds most commonly employed in the United Kingdom[20] and in the United States.[21] At this threshold, the outpatient procedure is not cost effective from a societal perspective (excluding productivity costs). The probability that the procedure is cost effective reaches 50% at a willingness to pay (WTP) of €68 000/QALY, and it only increases to 59% at €100 000/QALY. Hence, contrary to what is often assumed, in the main analysis no cost saving was associated with an outpatient procedure which was not cost effective unless a relatively high WTP is accepted.

Though this finding may be puzzling at first, there are several justifications. First, the estimates suggest that hospital hotel costs are lower for the first day of inpatient hospitalisation than for outpatient hospitalisation. This could be because of higher organisation demands associated with the outpatient procedure compared with the inpatient procedure, both being provided by the same hospitals or clinics. However, this is contradicted by a recent French retrospective study for different indications (sinonasal surgery), which found that the daily cost for same day surgery was 33% lower than for inpatient hospitalisation.[22] The discrepancy between that study and this one might be traced to the difference in indications or to differences in methodology, since this study was retrospective and carried out in a single centre. Secondly, in the inpatient arm, the mean initial hospital stay was relatively short (1.74 nights, *vs.* 0.26 for the outpatient arm). Indeed, the hospital stay was two nights in 71% of the patients in the inpatient arm and eight patients (10%) from the outpatient arm spent at least one night at the hospital. Therefore, elimination of the hospital day before the procedure might even give a larger advantage in this analysis to the inpatient arm as opposed to outpatient arm. Thirdly, the mean cost of the VCDs was higher for the outpatient arm (€167; median: 142; IQR: 130, 168)) than for the inpatient arm (€98; median: 130; IQR: 0, 138). However, regarding the follow up period, re-interventions or re-admissions were not related to the VCD use in both groups which is consistent with the current literature.[23]

On the other hand, these findings could be contested. Indeed, in the AMBUVASC trial, re-admissions only occurred in the outpatient arm. Excluding these re-admissions makes the outpatient procedure cost effective whatever the WTP for a QALY. There were three re-admissions and five re-interventions in the outpatient arm, *vs.* zero and one in the inpatient arm, respectively. Patients were never re-admitted for bleeding complications at the femoral puncture point, but rather for target limb complications during the peri-operative period. Furthermore, there was no re-admission or death within the first 24 h after discharge in the outpatient arm. Few trials in the literature provide peri-operative re-admission rates. Spiliopoulos *et al.* indicated a 30 day re-admission rate of 0.5% (3/652), and Akopian reported three treatment failures without the need for re-admission.[24,25] Definitely more data on re-admission and potential difference between outpatient and inpatient treatment are needed in the future to be conclusive.

Caution should be taken before generalising the findings. They may be driven by the specific organisation of the procedures in France, where outpatient procedures are performed in hospitals that also offer inpatient hospitalisation. In this trial, same day discharge interventions were thus performed in the outpatient departments of a hospital designed for inpatient treatment. This might have cause hospital costs of the outpatient procedure to be higher than for alternative organisations of this procedure. Other alternatives to outpatient hospitalisation might be considered such as ambulatory surgery centres or office based laboratory procedures.[26,27] Munnich *et al.*, for example, showed that ambulatory surgery centres reduced the intervention time by 25% when compared with hospitals.[28] In the United States, Jones[31] reported a proportionately greater increase in the number of peripheral vascular interventions (reported per 100 000 Medicare beneficiaries) conducted in office based laboratories (from 6.0 in 2006 to 37.8 in 2011) *vs.* outpatient hospital settings (184.7 in 2006 to 228.5 in 2011).[25] In 2010 Jain *et al.* reported the effect of office based procedures on case volume, office revenue, and the financial impact on the health care system.[29] Venous and arterial cases were performed. The authors concluded that office based procedures result in an increase in savings for the healthcare system. But this study was not controlled and the cost effectiveness of the procedures should still be proven from a societal perspective.

This study has limitations that are worth mentioning. First, the hotel cost estimates rely on national averages that may differ from specific hospitals' production costs and overestimate the cost of the outpatient procedure. The sensitivity analyses showed that a 10% decrease in hotel costs for the outpatient procedure would reverse the conclusion and make the outpatient procedure cost effective for relatively low values of the WTP per QALY. Yet, it cannot be ignored that top down costing may also overestimate production costs for the inpatient procedure

among those patients eligible for same day surgery. Exploring this issue would require conduct of a microcosting study for both the whole inpatient and outpatient procedure (including hospital stay), which could be very resource intensive. Secondly, QALYs are concerned with health related quality of life and survival outcomes: they do not consider patient satisfaction with the type of procedure they have undergone. Accounting for this satisfaction might reveal a difference between arms. This could not, however, be investigated because participating patients had accepted random assignment to one of the two arms, which might imply a selection bias with respect to their satisfaction with the particular procedure performed. Moreover, the interpretation of the results is based on an arbitrarily chosen threshold of €50 000: a different threshold might have led to an opposite conclusion. Nonetheless, the probability of the outpatient procedure being cost effective rises slowly with the threshold and only reaches 59% at €100 000/QALY. Additionally, in AMBUVASC each site was highly experienced with outpatient PAOD endovascular revascularisation. Consequently, these results could not be generalised to a centre with a lower outpatient experience. Finally, AMBUVASC was not blinded. Indeed, even if surgical interventions are frequently more difficult to blind than randomised clinical trials of drugs, some techniques exist to make blinding feasible in surgical studies.[30]

In conclusion, from a societal perspective, the approach followed in the AMBUVASC trial did not allow the conclusion that outpatient hospitalisation is cost effective compared with inpatient hospitalisation for the endovascular repair of patients with claudication at a willingness to pay threshold of €50 000/QALY. This result was mainly explained by the higher number of re-admissions in the outpatient arm. The findings depend on the specific organisation in France, where the two procedures are performed within the same institutions. Caution should thus be exercised before generalising to other contexts or countries. In addition, the costs differences were observed to be small, which makes them sensitive to the precision of the estimation of hospital hotel costs (other costs than those of the intervention). This calls for further research to investigate the reasons for re-admissions and to consolidate the estimation of the differences in initial hospital costs between outpatient and inpatient treatment before a definitive conclusion can be reached. Nevertheless, the study points out the importance of not too readily assuming that outpatient procedures are necessarily cost effective compared with inpatient procedures. Finally, outpatient hospitalisation appears as an alternative to conventional hospitalisation. The type of hospitalisation raises questions in term of safety, outcomes, devices, legal issues, and cost effectiveness and should be discussed in the upcoming guidelines.

CONFLICT OF INTEREST

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