Title page

Title: **M**ajor **A**dverse cardiac and cerebrovascular event & patients' **Q**uality of life after **E**ndoscopic Vein **H**arvesting as compared to open vein harvest (MAQEH): a pilot study

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ABSTRACT

Background: This is a prospective, comparative, pilot and follow-up (2 years post-op) study in patients undergoing coronary artery bypass surgery (CABG) where the long saphenous vein (LSV) was harvested either by the endoscopic technique (EVH) or open technique (OVH). Quality of life (QOL) and major adverse cardiac and cerebro-vascular event (MACCE) were assessed.

Methods: Alive patients who were initially part of a pilot study when EVH was introduced in our institution were included (n= 48 - EVH, n=49 -OVH). Patients were sent a QOL questionnaire (SF12v2) and their cardiologist & general practitioner were contacted to assess MACCE.

Results: Median follow-up was 32 & 33 months respectively. Three patients died (2 EVH, 1 OVH). Of the remaining 97 patients who were sent a questionnaire, 76% patients returned the form. More patients from the EVH group returned the QOL questionnaire (82% v/s 71%). Time taken to return to normal daily activities was much shorter in EVH - median 6 (2,30) weeks compared to OVH - median 9 (2, 50) weeks ($p<0.05$). QOL questionnaire revealed significant difference in physical score: 45.3 (10.2) for EVH group and 40.7 (11.0) for OVH group ($p<0.05$) at follow-up. There were no difference in mental scores (46.9 (10.5) v/s 49.2 (9.1), $p = 0.4$). There were no significant differences in MACCEs including death between the two groups (12.2% v/s 13.9%, $p = 0.5$).

Conclusion: EVH patients returned to normal daily activities faster than OVH patients and experienced better physical quality of life even after 2-years post-op with no increase in MACCE during follow-up.

Key words: Endoscopic vein harvest, quality of life, major adverse cardiac & cerebro-vascular event

Key Messages

What is already known about this subject?
There have been some concerns regarding MACCEs after EVH for CABG. Moreover, QOL after CABG has not been reported when based on the technique of LSV harvest

What does this study add?
This manuscript confirmed that MACCE rates were similar between EVH and OVH techniques of LSV harvest for CABG. In addition, is also showed that the physical aspect of the QOL was significantly better in patients who had EVH for LSV harvest as compared to OVH even 2 years after their surgery.

How might this impact on clinical practice?
This will serve as a pilot study to generate a randomized control trial to confirm these benefits. Once confirmed, patients will benefit from a better QOL without jeopardizing graft patency.

INTRODUCTION

Coronary artery bypass grafting (CABG) is recognised as one of the options in the management of patient with coronary artery disease. The short and long term outcomes after CABG are excellent with a very low mortality.[1]. However, the early morbidity from long saphenous vein (LSV) harvesting via the open technique (OVH) has been high with leg wound problems reported in significant number of patients.[2] and leg wound infection in up to 20%.[3]. The development of endoscopic vein harvesting (EVH) has been reported to be associated with better leg wound outcomes.[4,5,6]. This has been appraised by NICE (National Institute for Health and Care Excellence) and the latest NICE guidelines have endorsed the use of EVH.[7].

However, there were some initial concerns regarding vein graft patency.[8,9] but more recent meta-analysis have not supported these concerns.[10]. EVH was introduced to our practice as part of service improvement in 2012. The short term benefit of EVH as compared to OVH, in our population group has already been proven and included reduction in leg wound problems and infection, a reduction in leg wound pain and shorter in-hospital stay.[11]. The benefit of EVH has also been supported by the 2014 ESC/EACTS guidelines for myocardial revascularisation.[12].

Currently, there are no randomised control trials or large observational report of QOL after EVH reported in the literature.

The use of EVH is becoming more popular in the Western World. This technology was introduced in our Unit a few years ago and is now used in most patients as there is evidence that there has been a significant cost-benefit in our patient group.[11].

This study aimed to assess the intermediate outcome including MACCE and quality of life (QOL) in the EVH and a matched OVH group.

METHODS

Patients who were initially part of a prospective matched study comparing the initial experience with EVH to OVH (n=100) were included. These patients were at high risk of developing leg wound problems and had at least two of the following factors: female gender, age over 75 years, diabetes, body mass index - BMI > 28 kg/m^2, smoker and presence of peripheral vascular disease

(PVD). Fifty continuous patients who were suitable for EVH were selected for this modality of LSV harvest and were matched prospectively with 50 continuous patients who had OVH during the same time period. All patients who were still alive at the time of this current study (n=97) were sent a QOL questionnaire (SF12v2) and their cardiologist & general practitioner were contacted to assess MACCE based on clinical assessment but not angiography. EVH was performed using the Vasoview Haemopro II Endoscopic Vessel Harvesting System (Cardiovascular LLC, Wayne, New Jersey). All patients had their cardiac procedure with the use of the cardiopulmonary bypass machine.

This study was agreed by the Hospital's Research & Development Department and had the Ethical approval (NRES Committee South Central - Oxford, Ref 15/SC/0178). All patients consented for their cardiologist/ general practitioner to be approached to determine if there were any MACCE.

Continuous variables are expressed as mean (SD) or median (minimum, maximum) for Gaussian and skewed distributed data respectively. Group comparisons were carried out using the t-test or non-parametric (Mann-Whitney U) test accordingly. Categorical data are expressed as percentage and differences between the two groups assessed using the chi square (χ^2) test of independence. Tests were considered significant at $p \leq 0.05$. Statistical analyses were carried out in SPSS version 20 (IBM, SPSS package).

RESULTS

There were no significant differences in patients' pre-op characteristics (Table 1).

	EVH (n=50)	OVH (n=50)	p-Value
Age*, years	67.4 (10.6)	68.7 (8.6)	0.6
Male (%,n)	82%, 41	82%, 41	1
Patients > 75 years (%,n)	24%, 12	22%, 11	0.9
Non-diabetic (%,n)	60%, 30	60%, 30	1
Smokers (%,n)	18%, 9	14%, 7	0.6
PVD (%,n)	26%, 13	24%, 12	0.9

Impaired LVEF (%,n)	32%, 16	38%, 19	0.7
BMI > 28 kg/m^2 (%,n)	62%, 31	62%, 31	1
Elective (%,n)	54%, 27	58%, 29	0.8
Log EuroScore**	3.92 (0.88,33.63)	4.99 (0.88, 30.1)	0.6
Isolated CABG (%,n)	78%, 39	76%, 38	0.9

Table 1: The patients' pre-op characteristics. (EVH: Endoscopic Vein Harvest technique OVH: Open Vein Harvest technique, PVD: peripheral vascular disease, LVEF: left ventricular ejection fraction, BMI: body mass index, CABG: coronary artery bypass surgery.
*denotes mean (SD), **denotes median (minimum, maximum))

Median follow-up was 32 (28, 43) months and 33 (28,42) months for the EVH and OVH groups respectively (p=0.6). Three patients died (2 EVH, 1 OVH) during that period. Of the remaining 97 patients who were sent a questionnaire, 76% patients returned the form. Interestingly more patients from the EVH group returned the QOL questionnaire (82% v/s 71%).

The time taken to return to normal daily activities was much shorter in EVH - median 6 (2,30) weeks compared to OVH - median 9 (2, 50) weeks ($p<0.05$). QOL questionnaire revealed significant difference in physical score: 45.3 (10.2) for EVH group and 40.7 (11.0) for OVH group ($p<0.05$) at follow-up, Figure 1. There were no difference in mental scores (46.9 (10.5) v/s 49.2 (9.1), $p = 0.4$). There were no significant differences in MACCEs including death between the two groups (12.2% v/s 13.9%, $p = 0.5$). The MACCE reported for each group is listed in Table 2.

MACCE	Time to event
EVH group (n=41)	
Death	immediate post-op: multi-organ failure
Death	19 months post-op: pneumonia
Angina	10 months post-op
De-compensated cardiac failure	6 months post-op (poor LVEF pre-op)
Right occipital small infarct	2 weeks post-op

OVH group (n=36)	
Death	34 months post-op: heart failure
AF with de-compensated heart failure	3 months post-op
Angina - stenosis of OM	6 weeks post-op
Intra-cerebral haemorrhage	4 weeks post-op
Heart failure	3 months post-op

Table 2: MACCE (major adverse cardiac and cerebro-vascular event) for the two groups. (EVH: Endoscopic Vein Harvest technique, OVH: Open Vein Harvest technique, LVEF: left ventricular ejection fraction, AF: Atrial Fibrillation, OM: Obtuse marginal artery)

DISCUSSION

This is the first report on quality of life post CABG taking into account the modality of long saphenous vein harvest. Previously, QOL post CABG has been compared to PCI,[13,14] where no significant differences were reported between the two groups. The effect of on-pump and off-pump CABG on QOL has also been assessed and has been shown that there were no significant differences between these two groups.[15]. Longitudinal QOL assessment showed an important improvement in QOL after CABG.[16]. The effects of age on QOL in CABG have also been documented in the literature.[17,18] with the greatest benefit seen in the more elderly population. This current study assessed the QOL as a function of the type of LSV harvest (EVH v/s OVH). However, there was not a pre-procedure QOL assessment but given that the patients were selected continuously and that the two groups were matched on their pre-operative characteristics, the risk of any bias would have been minimal. The SF12v2 assessments showed a clear benefit at the time of follow-up (median around 32 months) in terms of physical performance, when EVH was used. There was no significant impact on mental performance at follow-up between the two techniques (EVH or OVH).

Persistent leg wound problems even months after CABG, have previously been reported,[19] with harvest site pain, numbness and dys-aesthesia. Similar findings were reported by Zhu et al as part of a sub-analysis in the RAPCO trial.[2]. In the initial study for the current study group, worst pain was also documented in the OVH arm when compared to the EVH arm.[11].

There have been some concerns regarding the patency of LSV grafts when EVH is used. These were initially highlighted in the sub-study of the ROOBY trial [8] and also with the PREVENT IV trial [9]. However, more recent data with the latest EVH technology suggested that LSV graft patency is not affected as compared to OVH.[10,20]. Similar outcomes have been reported when the LSV had been harvested by EVH for lower limb vascular procedures.[21]. In the current study, only a small percentage of patients post CABG had either an ischaemic event or evidence of blocked grafts on angiography: 2.4% (1/41) for EVH and 2.8% (1/36) for OVH.

Overall MACCE rates in this current study were 12.2% (EVH) v/s 13.9% (OVH). This rate is fairly similar to those reported in the NOBLE trial - 19% for CABG at 5 years.[22] Thus, within this small series, EVH use was not associated with an increased MACCE rate.

Limitations

This was a single centre, pilot study. Moreover, pre-operative QOL data was not available for both groups of patients. Treatment assignments were not blinded. Knowledge of treatment status may have affected QOL responses. QOL measures reflect a subjective assessment of health status; participants from diverse cultures may attach different significance to symptoms/limitations. Because of lack of randomization, such differences could have affected the scores. Many biologic and socioeconomic factors not included in this analysis may also impact QOL.

CONCLUSION

EVH patients returned to normal daily activities faster than OVH patients. The former also experienced better physical quality of life even after 2-years post-op with no increase in MACCE during follow-up when compared to OVH patients. However, given that is was only a pilot study involving a small number of patients, a larger randomised control trial would be beneficial to confirm these findings.

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Authors' contribution: This study was designed by HL, CM, KN & PK. Data was collected by an independent research nurse. HL, KN & AMN partook in the data interpretation. AMN carried out the data analysis .All the authors contributed to the manuscript writing and agreed the final version which is submitted

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Conflict of interest: HL has received educational grant from MAQUET to attend Cardiothoracic Surgical Meetings. There is no conflict of interests to be declared from the remaining authors.

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FIGURE LEGENDS

Figure 1: Physical scores (SF12v2) of the EVH and OVH groups