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ORIGINAL ARTICLE

Long-term outcomes in surgically ineligible patients managed with percutaneous coronary revascularization or medical therapy

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Abstract

The objective of the study was to report clinical outcomes of patients unsuitable for surgical coronary revascularization (CABG) treated with percutaneous revascularization (PCI) or medical therapy alone (MT). The decision to revascularize-patients referred for CABG but who are unsuitable should be made at Heart Team meetings. The clinical outcomes in this important patient subset are not known, and while cases are considered individually, these decisions are not guided by robust data. Clinical data were analyzed for patients referred to the Heart Team for consideration of CABG over a 4-year period in a UK tertiary referral center. Outcome data for those managed with urgent PCI or MT were considered over a further 3-year period. 133 patients were treated with PCI and 117 with MT. MACE at 30 days were no different between groups (MT 10.3% versus PCI 12.2%); however, at 1 year MACE were higher in the MT group (MT 39.3% versus PCI 26.7%, $P<0.01$). Log rank for MACE-free survival to 1 and 3 years was significantly lower in the MT group [HR 1.77 (0.60–1.11); $P<0.001$]. Residual SYNTAX was an independent predictor of death. MT [OR 1.75 (1.03–2.99); $P=0.04$] and a residual SYNTAX score [OR 6.45 (2.53–16.45); $P<0.001$] were independent predictors of MACE at 1 year in the whole group. Our data reveal better outcomes in patients treated with PCI over MT at 1–3 years in CABG-ineligible patients. Patients without complete revascularization have worse outcomes.

Keywords PCI · Risk stratification · Drug-eluting stent

Introduction

Percutaneous coronary intervention (PCI) is often performed as an alternative treatment modality in addition to optimal medical therapy in patients considered ineligible for surgical revascularization (CABG) due to co-morbidities [1]. This patient group is normally considered to be at high risk and surgical ineligibility has been identified as an independent risk factor for adverse outcomes [2]. Real-world cohorts such as these are not generally included in randomized controlled trials and their long-term outcomes are poorly understood.

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Unlike surgically "fit" patients who can expect a mortality benefit from CABG versus conservative management [3], the longevity or incidence of major clinical adverse events (MACE) in CABG-ineligible patients who are managed with an alternative strategy such as PCI or optimal medical therapy in the current era has not been previously reported. The decision regarding revascularization strategy is most appropriately determined by a multidisciplinary assessment by the "Heart Team". While scoring systems exist to aid decision making, these are generally used to compare the appropriateness of CABG versus PCI, rather than PCI versus MT. The Euroscore II validated for patients undergoing CABG uses clinical criteria to assess risk and a high Euroscore II may make non-surgical management more attractive, although not necessarily safer. Anatomical scores such as SYNTAX score have an important relationship with clinical outcome in patients being revascularized with PCI [4, 5]. Patients within the highest SYNTAX score tertile have higher rates of death, MI and repeat revascularization compared to those undergoing PCI in the lowest tertile [6] or those undergoing

CABG with the same extent of disease [4, 7]. However, this relationship does not necessarily hold true for all patients with "high risk" coronary anatomy. Unprotected left main (LM) disease treated by PCI has been shown to have outcomes similar to surgery in low and intermediate SYNTAX tertiles in large trials [7–10]. This includes the EXCEL trial which demonstrated non-inferiority of PCI to CABG at 3 years in patients with LM disease with SYNTAX scores less than 33 [10]. However, PCI was inferior to CABG at 5 years in the NOBLE trial which included patients with SYNTAX scores over 32 [11]. In both of these important trials, patients' coronary anatomy was deemed "suitable" for PCI, and there was an agreement that PCI and CABG have equipoise at a Heart Team meeting. As such, PCI now has a Class IIa recommendation in patients with multi-vessel coronary disease who cannot undergo CABG [12]. However, there is little or no evidence to determine any residual benefit of PCI over medical therapy alone within surgically ineligible patients or understanding of the outcomes of patients whose anatomy is unsuitable for PCI. Inevitably, the 'Heart Team' may conclude that some patients are best managed medically but the reasons for this are pragmatic rather than evidence based. The aim of our study was to consider the clinical and anatomical characteristics and outcomes of a cohort of patients deemed surgically ineligible presenting to a single center over a 4-year period. Furthermore, we aimed to identify those factors associated with an adverse outcome in order to determine whether there was any benefit of PCI over those selected for treatment with medical therapy alone in this difficult patient cohort.

Methods

This was an observational cohort study to investigate the outcomes of patients referred for CABG but turned down by a cardiac surgeon at the Heart Team meeting on the basis of co-morbidities. The primary outcome was the composite rate of major adverse clinical event (MACE, defined as all-cause mortality; cardiac death, myocardial infarction, MI; urgent revascularization; and stroke) in patients treated with PCI compared to MT at 30 days and 1 year. Patient data were retrieved retrospectively from the archives of the weekly Heart Team meeting at our center (which receives referrals from a wide range of centers in the south east of England) from 2008 to 2012. During this period, the Heart Team used an algorithm to guide decisions regarding revascularization in patients (see Fig. 1). We identified patients being discussed at the Heart Team meeting where there was a consensus that CABG was the optimal revascularization modality. Patients were included if they were considered unsuitable for CABG by at least two surgeons. MT was chosen over PCI when there was a perceived lack of long-term benefit of PCI or the anatomy was considered unattractive.

Clinical data at the time of surgical ineligibility were considered. For the purposes of the study, cognitive impairment was defined as a documented history of dementia or reduced mental test performance prior to the index hospital admission. Reduced mobility was defined as documented severe limitation of physical mobility prior to any recent acute hospitalization due to musculoskeletal or neurological deficiency. Peripheral vascular disease (PVD) was defined as a documented history of intermittent claudication or lower limb vascular surgery due to peripheral atherosclerosis. A recent acute coronary syndrome (ACS) was defined as an ACS within 30 days preceding coronary angiography. Those who had not experienced a recent ACS were considered to be stable patients (cases of acute ST elevation myocardial infarction were not included in this study). Valve disease was defined as the presence of chronic aortic or mitral stenosis or incompetence that was at least moderate in severity on echocardiography within 30 days of coronary angiography. The reasons cited for surgical ineligibility were also recorded. EuroSCORE II (ESII) and SYNTAX scores were calculated. The mean values were determined but patients were also stratified into low (0–6) or high (> 6) clinical risk categories on the basis of (ESII); and low (0–22), medium (23–32) or high (> 33) anatomical complexity on the basis of SYNTAX score. Complete revascularization (CR) was assessed by calculating SYNTAX score after PCI (residual SYNTAX score) and defined as having a residual SYNTAX score of 0. Medical records were then analyzed to determine the 30 day and 1 year major adverse cardiac event (MACE) rate. Mortality data were corroborated by linkage of patients' National Health Service numbers to the Office of National Statistics, which records live status and the date of death for all deceased patients. Myocardial Infarction (MI) was defined as presentation to hospital with typical symptoms, ECG changes and a rise in serum troponin I over two standard deviations of the normal range. Stroke was defined as a persistent neurological defect with consistent changes seen on neuroimaging. The timing of adverse events was determined from the commencement of treatment and an event-free survival time was calculated up to a maximum of 36 months for all patients. Analysis was performed on an intention to treat basis and emergency revascularization in the MT group was considered as adverse event.

Ethics

The data were collected as part of the national cardiac audit and all patient identifiable fields were removed prior to analysis. The local ethics committee advised us that formal ethical approval was not required.

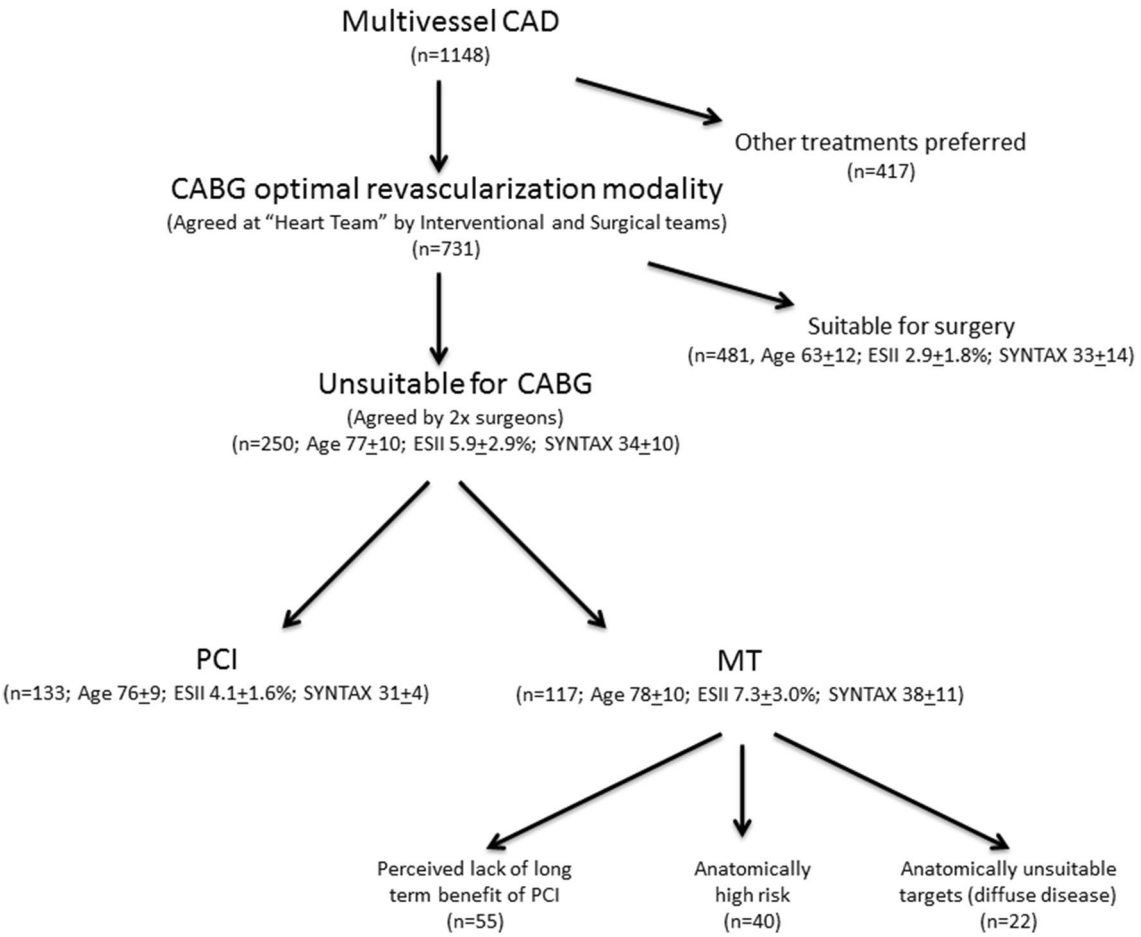


Fig. 1 Decision-making algorithm for revascularization of patients at the Heart Team meeting. Patients deemed ineligible for coronary artery bypass grafting (CABG) and treated with either percutaneous coronary intervention (PCI, $n=131$) or medical therapy (MT, $n=117$) were included in the analysis

Statistical analysis

Normality of distribution was assessed using the Shapiro–Wilks test. Clinical characteristics of patients at baseline, reasons for surgical turndown, medical treatments and MACE data at 30 days and 1 year were compared in the PCI and MT groups using the Pearson Chi-square test. We calculated Kaplan–Meier product limits for cumulative probability of MACE-free survival to 3 years and used the log-rank test for evidence of a statistically significant difference between the groups. Time was measured from the PCI procedure or designation to treatment with medical therapy alone to the outcome (composite MACE). Cox proportional hazards modeling was used to determine the factors associated with MACE over 1 year and to determine the hazard ratios for the effect of PCI compared to MT on the rate of composite MACE at 1 year within subgroups by clinical criteria. Bivariate analysis of the entire cohort was undertaken to determine predictors for MACE at 1 year using Fisher's exact probability test. Stepwise regression modeling was then performed using a backward elimination technique in order to determine the strongest independent predictors of outcome at 1 year.

Propensity score matching

With significant imbalances in baseline characteristics between the PCI and MT groups, we used propensity score matching to assemble a well-balanced cohort of patients. All clinically relevant baseline characteristics ($n=27$) were included as covariates. Propensity scores were used to perform 1:1 nearest neighbor matching within a caliper of 0.20 standard deviations of the logit of the estimated propensity score. This caliper width has shown to result in optimal estimation of risk difference [A].

Balance was verified by assessing standardized differences between the PCI and MT groups for all variables in the pre- and post-matched cohorts. An absolute standardized difference of 0% on a covariate indicates no residual

bias for that covariate and a difference below 10% suggests inconsequential bias.

The occurrence of MACE in both the PCI and MT groups was compared at both 6 months and 1 year in the propensity matched cohort using the Pearson Chi-square test.

Results

Clinical characteristics of surgically ineligible patients

During the study period, 248 patients were determined to be surgically ineligible by the Heart Team: 131 (53%) of whom were managed with PCI and 117 (47%) with medical therapy alone. The mean age in the PCI group was 76 ± 9 and 78 ± 10 in the MT group ($P = 0.6$). Mean ESII was 4.1% in the PCI group and 7.3% in the MT group ($P = 0.0046$). The demographics and baseline clinical characteristics of each group are summarized in Table 1. Higher rates of male sex, cognitive impairment, reduced mobility, PVD, 3VD, CTO, prior CABG, and recent ACS were seen in the MT group. Higher rates of hypertension, sinus rhythm and LM disease were seen in the PCI group. The coronary anatomical characteristics are summarized in Table 2. Isolated LMS disease was present in 12% of the PCI group ($n = 16$) and 10% of the medical group ($n = 12$; $P = 0.39$ NS) indicating that this was only more prevalent in the PCI group in the context of multi-vessel disease. The rate of complete revascularization was significantly less than those in the highest SYNTAX tertile at baseline (see Table 2).

Reasons for surgical ineligibility

The reasons cited for surgical ineligibility at the Heart Team meeting were similar in both groups of patients (see Fig. 2). The majority of patients were excluded because of perceived frailty after assessment by a cardiac surgeon than because of any objective co-morbid pathology. A small minority of patients were not surgical candidates because of multiple co-morbidities, anatomical reasons or reduced life expectancy. More patients were treated with MT because of a lack of symptoms than with PCI after being turned down for CABG ($P = 0.009$). As this study was designed to assess outcomes in real-world practice, no patients were excluded in the outcome analysis.

Medical therapy

Medical treatment data at the time of discharge from hospital or at the time of patients' meeting the primary endpoint were available for 100% of the study patients. There were no differences between PCI and MT groups indicating

Table 1 Baseline characteristics

	PCI (%)	Med (%)	*P*
Male	79/131 (60.3)	88/117 (75.2)	0.01
Age >75	71/131 (54.2)	77/117 (65.8)	0.06
HTN	112/131 (85.5)	80/117 (68.4)	0.001
Smoking	60/131 (45.8)	63/117 (53.8)	0.21
DM	35/131 (26.7)	74/117 (31.6)	0.4
Chol	82/131 (62.6)	74/117 (63.2)	0.92
eGFR<40	35/131 (26.7)	23/117 (19.7)	0.19
HDx	14/131 (10.7)	6/117 (5.1)	0.11
EF<40	52/131 (39.7)	54/117 (46.2)	0.3
COPD	19/131 (14.5)	20/117 (17.1)	0.58
Stroke	16/131 (12.2)	23/117 (19.7)	0.11
Cognitive Impairment	0/131 (0.0)	11/117 (9.4)	<0.001
Reduced mobility	22/131 (16.8)	49/117 (41.9)	<0.001
PVD	11/131 (8.4)	26/117 (22.2)	0.002
Neoplaisia	5/131 (3.8)	11/117 (9.4)	0.07
3VD	98/131 (74.8)	100/117 (85.5)	0.04
LM	60/131 (45.8)	29/117 (24.8)	<0.001
CTO	57/131 (43.5)	66/117 (56.4)	0.04
Prior CABG	52/131 (39.7)	66/117 (56.4)	0.009
Recent ACS	76/131 (58.0)	91/117 (77.8)	<0.001
Valve disease	25/131 (19.1)	23/117 (19.7)	0.91
SR	112/131 (85.5)	83/117 (70.9)	0.005
PPM	14/131 (10.7)	6/117 (5.1)	0.11
ESII>6	30/131 (22.9)	49/117 (41.9)	0.001

ACS acute coronary syndrome, *CABG* coronary artery bypass grafting, *Chol* hyperlipidaemia, *COPD* chronic obstructive pulmonary disease, *CTO* chronic total occlusion, *CVA* stroke, *DM* diabetic mellitus, *EF* ejection fraction, *ESII* euroscore II, *eGFR* estimated glomerular filtration rate, *HDx* hemodialysis, *HTN* hypertension, *LM* left main stem disease, *PPM* permanent pacemaker, *PVD* peripheral vascular disease, *SR* sinus rhythm, *3VD* triple vessel disease

Table 2 Coronary anatomical characteristics

	PCI (%)	Med (%)	*P*
SYNTAXI	33/131 (25.2)	17/117 (14.5)	0.04
SYNTAXII	60/131 (45.8)	46/117 (39.3)	0.3
SYNTAXIII	38/131 (29.0)	54/117 (46.2)	0.005
	Baseline SYNTAX (pre PCI)	Residual SYNTAX (post PCI)	CR (%)
SYNTAXI	19 ± 2	2 ± 1	29/33 (87.9)
SYNTAXII	30 ± 3	6 ± 1	53/60 (88.3)
SYNTAXIII	43 ± 5	19 ± 16	22/38 (57.9)*
Mean	31 ± 4	9 ± 8	104/131 (79.4)

CR complete revascularization, *Med* medical therapy, *PCI* percutaneous coronary intervention

*$p = 0.0001$, CR rate SYNTAXIII group compared to SYNTAXI + II

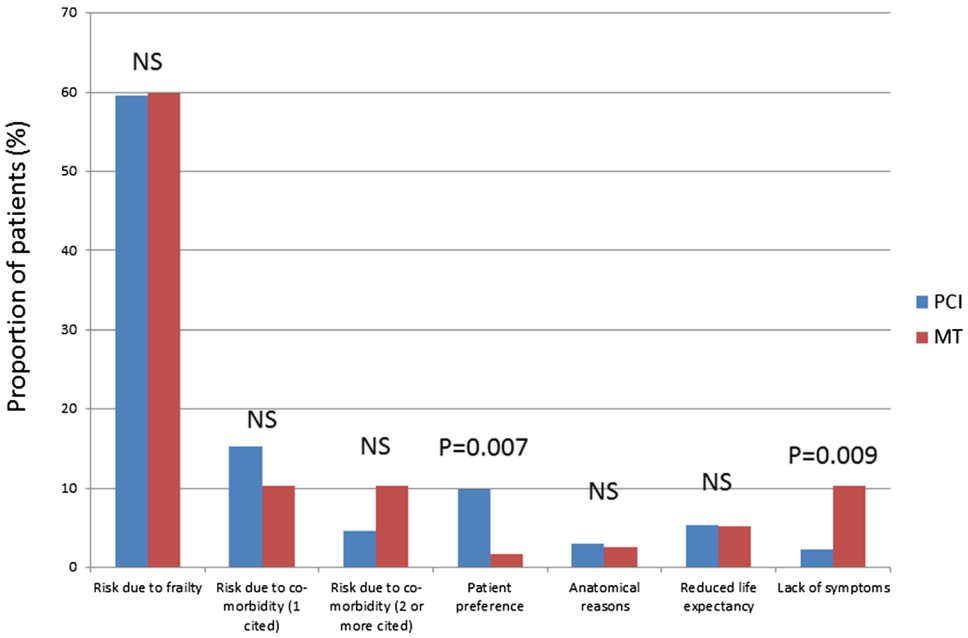


Fig. 2 Reasons for surgical turndown. The majority of patients were excluded from surgery due to subjective frailty or 1 or more co-morbidities. Patients were more likely to be managed with percutaneous coronary intervention (PCI) if they refused to have surgical revascularization ($P=0.007$, Chi-squared test), whereas they were more likely to be managed with medical therapy alone (MT) if their symptoms were well controlled ($P=0.009$, Chi-square test)

that revascularization was the only difference in treatment between groups (see Fig. 3).

Percutaneous coronary intervention

PCI success was considered to be absence of residual stenosis within the treated segment with TIMI 3 flow and was achieved in 129/131 patients (98%). Two procedural deaths were observed.

Clinical outcomes at 30 days and 1 year

The overall MACE rate in the PCI group was not significantly different from the medical treatment group at 30 days (see Table 3). More patients suffered stroke in the PCI group ($n=5$; 3.8%) all of which were periprocedural (within 24 h); however, there were no recorded patients with stroke in the medically managed group, making this a difficult comparison given the sample size.

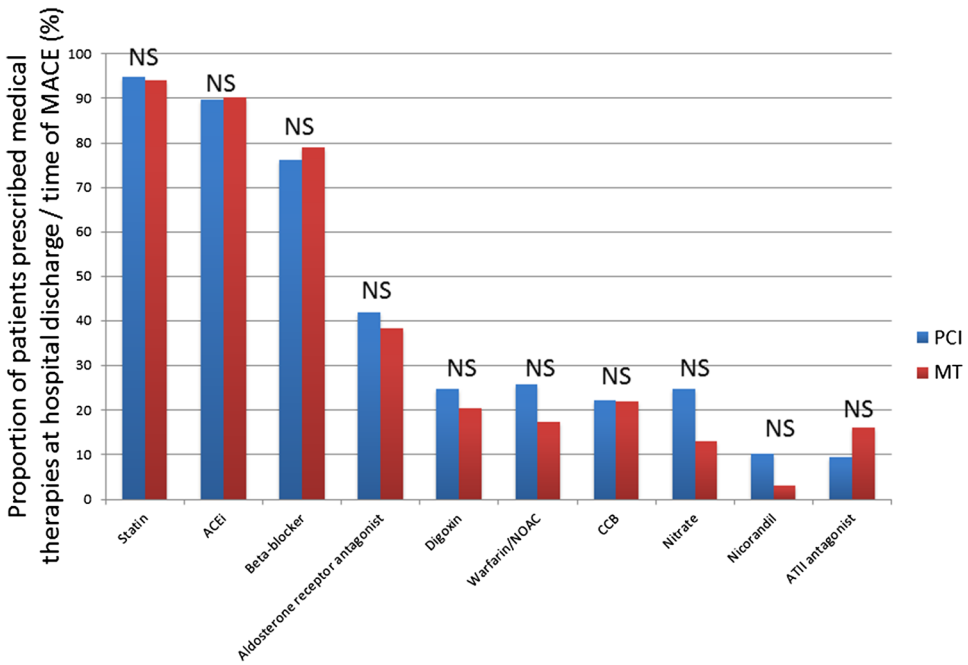


Fig. 3 Medical treatment of patients managed with percutaneous coronary intervention (PCI) or medical therapy alone (MT). There was no difference in prescribed medical treatments between the groups of patients for any class of commonly prescribed cardiac medication

Table 3 Summary of 30 days and 1 year outcome

	Total MACE (%)	Death (all cause, %)	Death (cardiac, %)	MI (%)	Repeat/urgent revascularisation (%)	Stroke (%)
Total (3 days)	28/248 (11.2)	11 (4.4)	8 (3.2)	14 (5.6)	5 (2.0)	5 (2.0)
Medical (3 days)	12/117 (10.3)	5 (4.2)	5 (4.3)	8 (6.8)	3 (2.6)	0 (0)
PCI (30 days)	16/131 (12.2)	6 (4.5)	3 (2.2)	6 (4.6)	2 (1.5)	5 (3.8)
Total (1 year)	81/248 (32.7)	45 (18.1)	25 (10.1)	17 (6.9)	25 (10.1)	5 (2.0)
Medical (1 year)	46/117 (39.3)	31 (26.5)	22 (18.9)	14 (12.0)	11 (9.4)	0 (0)
PCI (1 year)	35/131 (26.7)*	14 (10.7)*	3 (2.3)*	3 (2.3)*	14 (10.7)	5 (3.8)

*$P < 0.01$ PCI vs. MT

At 1 year, the total MACE rate was significantly lower in the PCI group (ARR 12.6%; OR 0.5627; 95% CI 0.3292 to 0.9612; NNT = 8; $P < 0.05$ Chi-squared). There were significantly lower rates of overall death ($P = 0.001$), cardiac death ($P < 0.0001$) and myocardial infarction ($P = 0.003$) in the PCI group. There were no differences in urgent revascularization rates between the groups ($P = 0.76$).

Multivariate analysis of the entire cohort revealed that independent predictors of composite MACE at 1 year were allocation to medical therapy (OR 1.75, CI 1.03-2.99, $P = 0.04$) and having a residual SYNTAX score greater than or equal to 33 (OR 2.72, CI 1.80-5.95, $P = 0.001$). Complete revascularization (79% of those undergoing PCI) was associated with lower MACE at 30d (OR 0.27, CI 0.09-0.81, $P = 0.02$) and 1y (OR 0.23, CI 0.09-0.57, $P = 0.002$) but several subgroups were less likely to have CR including those with CTOs (46%) and those with third tertile SYNTAX anatomy at baseline (58%). The presence of CTOs was not associated with MACE in either the PCI (OR 1.12, CI 0.52-2.46, $P = 0.76$) or MT groups (OR 0.65, CI 0.31–1.38, $P = 0.26$) at 1 year.

MACE-free survival to 3 years

Follow-up data were available to 3 years for 100% of the study patients and is presented in Fig. 4. Kaplan–Meier analysis revealed significantly worse outcomes in the MT group (14.5% MACE-free survival at 3 years) compared to the PCI group (51.9% MACE-free survival at 3 years) with the curves continuing to diverge between 1 and 3 years (HR 1.77, CI 0.60–1.11, $P < 0.0001$).

Subgroup analysis by clinical criteria

When comparing the PCI and MT groups separately, subgroup analysis revealed that numerous clinical factors were associated with increased MACE at 1 year in the medical therapy group. The only anatomical factor that predisposed to MACE in this group was the presence of LM disease (Table 4). In contrast, among patients managed with PCI, there was a relationship between SYNTAX tertile and MACE at 1 year. When comparing outcomes by treatment modality when patients were grouped by clinical or

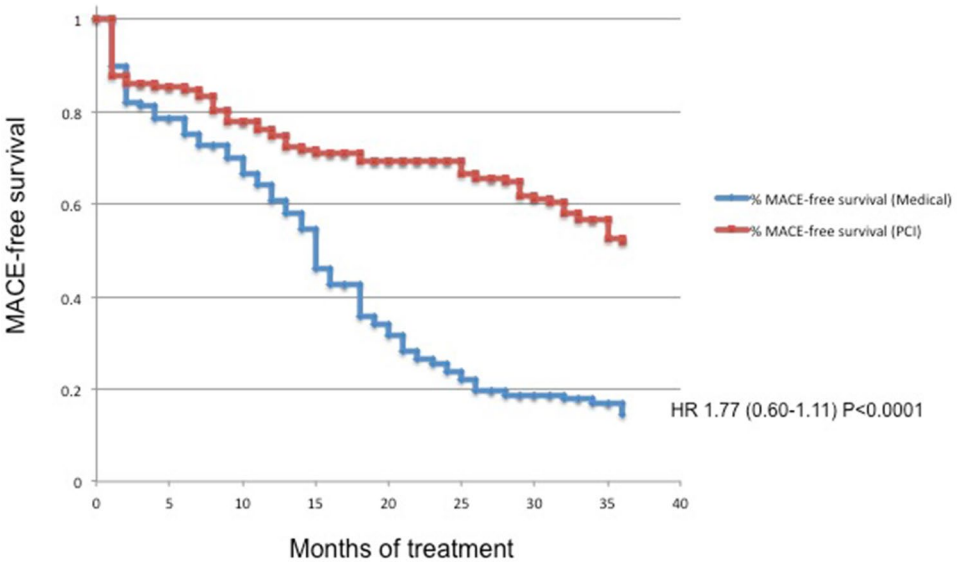
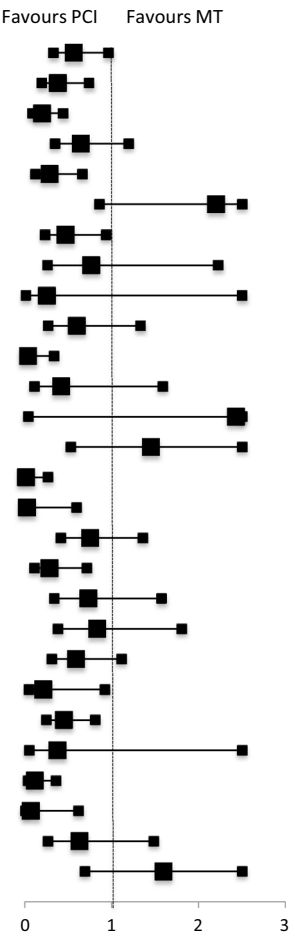


Fig. 4 Kaplan–Meier curve plotting major adverse clinical event (MACE)-free survival to 3 years in patients managed with percutaneous coronary intervention (PCI) versus medical therapy alone (MT). MACE-free survival was significantly worse in the medically managed patient group compared to the PCI group [hazard ratio (HR) 1.77 (0.60–1.11) $P < 0.0001$]

Table 4 Subgroup analysis of MACE-free survival in patients managed with percutaneous coronary intervention (PCI) versus medical therapy alone (MT)

	MT			PCI			MT vs. PCI		
	MACE rate	OR (CI)	P	MACE rate	OR (CI)	P	N	OR (CI)	P
Total MACE 1Y	46/117			35/131			81	0.6 (0.3-1.0)	0.0355
Male	40/88	3.2 (1.2-8.6)	0.0217	19/79	0.7 (0.3-1.6)	0.3961	167	0.4 (0.2-0.7)	0.0043
Age>75	35/77	2.2 (1.0-5.0)	0.0619	10/71	0.2 (0.1-0.5)	0.0006	148	0.2 (0.1-0.4)	0.0001
HTN	29/80	0.7 (0.3-1.5)	0.3193	30/112	1.0 (0.3-3.1)	0.9659	192	0.6 (0.3-1.2)	0.1624
Smoking	26/63	1.2 (0.6-2.5)	0.6404	10/60	0.4 (0.2-0.8)	0.019	123	0.3 (0.1-0.7)	0.0035
DM	15/37	1.0 (0.5-2.4)	0.8537	21/35	8.8 (3.6-21.2)	<0.0001	72	2.2 (0.9-5.6)	0.101
Chol	29/74	1.0 (0.5-2.1)	0.9706	19/82	0.6 (0.3-1.4)	0.2372	156	0.5 (0.2-0.9)	0.0319
eGFR<40	15/23	3.2 (1.2-8.1)	0.0166	19/35	5.9 (2.5-14.0)	<0.0001	58	0.8 (0.3-2.2)	0.6207
HDx	6/6	23.0 (1.3-418.0)	0.0343	11/14	14.2 (3.7-55.0)	0.0001	20	0.3 (0.0-5.7)	0.3869
EF<40	23/54	1.3 (0.6-2.7)	0.5021	16/52	1.4 (0.6-3.1)	0.3961	106	0.6 (0.3-1.3)	0.2085
COPD	12/20	2.8 (1.0-7.5)	0.0424	1/19	0.1 (0.0-1.0)	0.0493	39	0.0 (0.0-0.3)	0.0034
CVA	12/23	0.9 (0.8-4.8)	0.1629	5/16	1.3 (0.4-4.0)	0.6625	39	0.4 (0.1-1.6)	0
Cognitive Imp.	3/11	0.5 (0.1-2.2)	0.3958	0/0	2.7 (0.1-140.0)	0.6188	11	2.4 (0.0-148.4)	0.6724
Reduced mobility	20/49	1.1 (0.5-2.4)	0.778	11/22	3.5 (1.4-9.2)	0.0091	71	1.5 (0.5-4.0)	0.4715
PVD	20/26	8.3 (3.0-23.1)	<0.0001	0/11	0.1 (0.0-1.8)	0.1218	37	0.0 (0.0-0.3)	0.0046
Neoplaisia	9/26	8.4 (1.7-40.9)	0.0085	0/5	0.2 (0.0-4.3)	0.3302	16	0.0 (0.0-0.6)	0.0228
3VD	37/100	0.5 (0.2-1.5)	0.2185	30/98	2.5 (0.9-7.0)	0.0895	198	0.8 (0.4-1.4)	0.3428
LM	18/29	3.5 (1.5-8.4)	0.0049	19/60	1.6 (0.7-3.5)	0.241	89	0.3 (0.1-0.7)	0.0076
CTO	23/66	0.7 (0.3-1.4)	0.2614	16/57	1.1 (0.5-2.5)	0.7589	123	0.7 (0.3-1.6)	0.4212
Prior CABG	23/66	0.7 (0.3-1.4)	0.2614	16/52	1.4 (0.6-3.1)	0.3961	118	0.8 (0.4-1.8)	0.6402
Recent ACS	40/91	2.6 (1.0-7.1)	0.0601	24/76	1.8 (0.8-4.2)	0.1422	167	0.6 (0.3-1.1)	0.1026
Valve	9/23	1.0 (0.4-2.5)	0.9838	3/25	0.3 (0.1-1.1)	0.0762	48	0.2 (0.0-0.9)	0.0385
SR	40/83	4.3 (1.6-11.6)	0.0034	33/112	3.4 (0.8-15.8)	0.1113	195	0.4 (0.2-0.8)	0.008
PPM	4/6	3.3 (0.6-18.7)	0.1803	6/14	2.3 (0.7-7.1)	0.1569	20	0.4 (0.0-2.8)	0.3365
ESII>6	28/44	5.3 (2.4-12.1)	0.0001	5/30	0.5 (0.2-1.4)	0.163	74	0.1 (0.0-0.4)	0.0002
SYNTAXI	6/19	0.7 (0.2-1.9)	0.4525	0/33	0.0 (0.0-0.4)	0.0119	52	0.0 (0.0-0.6)	0.0171
SYNTAXII	15/46	0.6 (0.3-1.4)	0.2333	14/60	0.7 (0.3-1.6)	0.4218	106	0.6 (0.3-1.5)	0.2901
SYNTAXIII	25/54	1.7 (0.8-3.6)	0.1539	21/38	8.5 (3.5-20.2)	0.0006	92	1.6 (0.7-3.7)	0.2744



ACS acute coronary syndrome, *CABG* coronary artery bypass grafting, *Chol* hyperlipidaemia, *COPD* chronic obstructive pulmonary disease, *CTO* chronic total occlusion, *CVA* stroke, *DM* diabetes mellitus, *EF* ejection fraction, *ESII* euroscore II, *eGFR* estimated glomerular filtration rate, *HDx* hemodialysis, *HTN* hypertension, *LM* left main stem disease, *PPM* permenant pacemaker, *PVD* peripheral vascular disease, *SR* sinus rhythm, *3VD* triple vessel disease

anatomical factors, multiple subgroups had more favorable outcomes at 1 year when treated with PCI over MT.

Matched PCI and MT cohorts

After matching, the baseline characteristics were comparable between the PCI and MT groups (Table 5). Our propensity score matching reduced standardized differences for all observed covariates below 10% in absolute value, demonstrating substantial improvement in covariate balance across the two groups (Fig. 5). While there was no difference in MACE at 6 months between the PCI and MT groups (PCI 5/54 vs. MT 10/54, OR 0.45, 95 CI 0.14–1.42, $P=0.16$), MACE were significantly lower in the PCI group at 1 year (PCI 11/54 vs. MT 25/54, OR 0.30, 95 CI 0.13–0.70, $P=0.004$).

Discussion

Not every patient with multi-vessel coronary artery disease is necessarily suitable for either CABG or PCI. The decision to undertake PCI in patients who are deemed unfit for CABG typically follows a multidisciplinary discussion taking numerous clinical and anatomical factors into consideration. Part of this decision-making process is a risk–benefit assessment, with the complexity of the PCI procedure (and potential complications) being weighed against the putative benefits of symptom-relief and an improved quality of life. There has not previously been any data to support a mortality benefit in this population. Furthermore, the outcome of patients with severe coronary disease who are not revascularized and managed conservatively has not been previously demonstrated. Data collection from this population is

Table 5 Baseline characteristics after propensity matching

	PCI ($n=54$) (%)	MT ($n=54$) (%)	P value
Male	41 (75.9)	39 (72.2)	0.52
Age > 75 years	34 (63.0)	33 (66.7)	0.84
Hypertension	43 (79.6	43 (79.6)	1.00
Smoking	26 (48.1)	25 (46.3)	0.85
Diabetes mellitus	15 (27.8)	17 (31.5)	0.39
Hypercholesterolaemia	34 (63.0)	32 (59.3)	0.56
eGFRc40	25 (46.3)	24 (44.4)	0.85
COPD	9 (16.7)	9 (16.7)	1.00
Stroke	7 (13.0)	8 (14.8)	0.57
Cognitive impairment	0 (0)	0 (0)	–
Reduced mobility	16 (29.6)	17 (31.5)	0.84
PVD	9 (16.7)	7 (13.0)	0.4
Neoplasia	4 (7.4)	4 (7.4)	1.00
3VD	43 (79.6)	43 (79.6)	1.00
LMS disease	15 (27.8)	16 (29.8)	0.83
CTO	27 (50.0)	27 (50.0)	1.00
Prior CABG	24 (44.4)	25 (46..3)	0.85
Recent ACS	36 (88.7)	38 (70.4)	0.53
Valve disease	13 (24.1)	14 (25.9)	0.82
Sinus rhythm	41 (75.9)	40 (74.1)	0.82
PPM	4 (7.4)	3 (5.6)	0.46
SYNTAX score I	14 (25.9)	12 (22.2)	0.65
SYNTAX score II	25 (46.3)	26 (18.1)	0.85
SYNTAX score III	15 (27.8)	16 (29.6)	0.83

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typically hindered by significant follow-up bias because of patients' high mortality rate and because multiple medical specialists may be involved in their care. We report from our high-risk patient group that MACE-free survival is significantly better in those treated with PCI compared to those managed medically, although only after 30 days.

The optimal treatment modality for high-risk patients with myocardial ischemia is not known, particularly as these patients are typically deemed ineligible for entry into clinical trials. The AWESOME trial [13] compared survival in high risk patient groups with medically refractory ischemia randomized to CABG or PCI. The trial found no difference between survival overall but PCI had a survival advantage over CABG in patients with prior CABG within a registry cohort who were allocated to PCI rather than CABG because of physician or patient choice [14]. Patients with a history of prior CABG were also more likely to be selected for PCI than redo CABG in physician-selected and patient choice-directed registries by a 2:1 ratio. Within both these registries, medical therapy was chosen in roughly half the number of patients compared to PCI, although the outcomes in this group were not reported. Likewise, a large international European registry of patients deemed ineligible for a clinical trial found that patients had better 1 year survival when treated with PCI versus CABG [15]. Although 28% of these patients were managed medically, the outcomes of these patients were not reported making it unclear whether this was an optimal therapy. In contrast, our registry revealed that prior CABG had no impact on outcome in either patients treated with MT or PCI. Furthermore (with the exception of patients with significant LM disease), anatomical factors have no predictive power in determining the outcome of patients treated medically.

The factors determining surgical ineligibility and treatment modality in our cohort (most commonly patient frailty) reflects a subjective rather than score- based method for decision-making. There may be a reasonable body of evidence to support non-surgical management of patients who are older with higher surgical risk scores [13–15]; however, our data would suggest that patients with certain co-morbidities are also less likely to be offered revascularization. This includes patients whose symptoms are well controlled but clinical factors such as the presence of AF or cognitive impairment may also rightly sway decision making against revascularization because of risks related to bleeding [16]. Interestingly, ESII (which does not rank disease severity in most of its scoring criteria, nor does it incorporate a frailty index) was accurate at predicting procedural mortality in patients undergoing PCI (ESII 4.1%; 30 days mortality 4.5%) but overestimated short-term outcome in those managed medically (ESII 7.1%; 30 days mortality 4.2%). While short-term outcomes are similar, the difference in clinical outcome between patients who were revascularized and those treated with medical therapy alone is marked. This emerges around 6 months after treatment (Fig. 4). Cardiac death accounted for the majority of events in both groups. The underlying reason for the more favorable outcomes in patients who are revascularized cannot be determined from this study given the unmatched patient groups and relatively small sample size; however, the results are intriguing and hypothesis generating. As such, the independent relationship between adverse outcomes and treatment modality suggests that PCI may result in better long-term outcome in these patients. Furthermore, residual SYNTAX score (an index of incomplete revascularization) was also independently associated with MACE at 1 year. Taken together, this supports the hypothesis that PCI with complete revascularization may confer a mortality benefit compared to MT in this population.

A number of studies now have shown that patients with the greatest predicted benefit from revascularization are

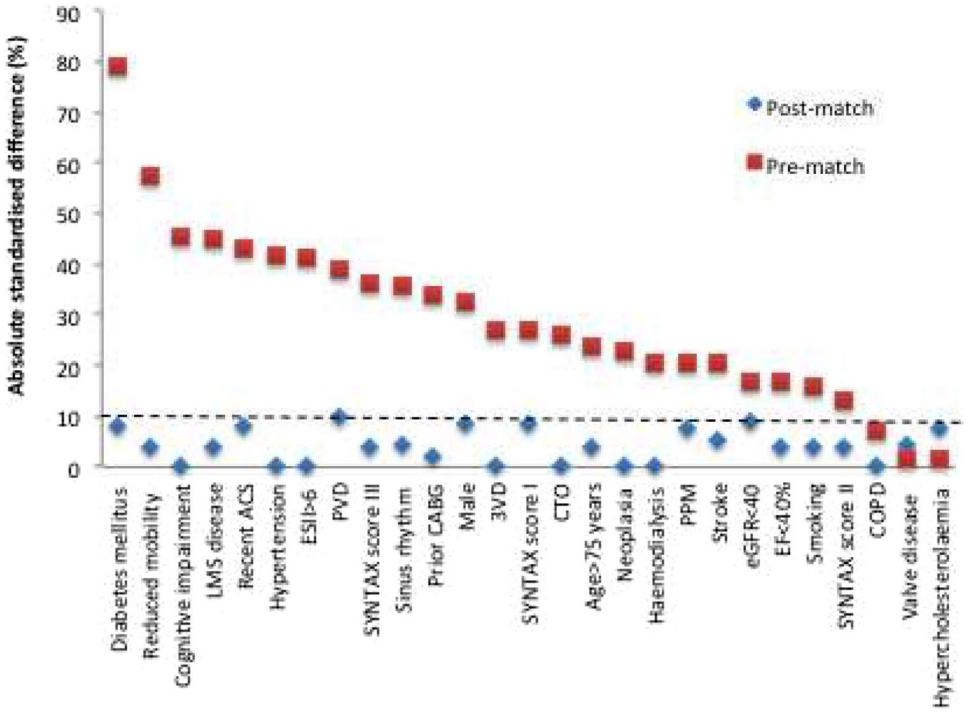

Fig. 5 Love plot for absolute standardized differences for baseline covariates between patients managed with PCI or MT, before and after propensity score matching

paradoxically the least likely to be revascularized [17–20]. The poor outcomes of patients treated medically in our cohort are consistent with those of other trials of patients with severe coronary disease [21–23]. Among 4491 patients treated medically within the ACUITY trial, those with SYNTAX scores above 8 had particularly high adverse event rates, indicating the important relationship between coronary disease severity and clinical outcome in the absence of revascularization [24]. The value of complete revascularization by PCI in patients with multivessel CAD remains a source of considerable debate [25–27]. However, these results are consistent with other studies where complete revascularisation has been associated with improved outcomes, albeit in lower risk patient groups [28].

Limitations of this study

It is important to emphasize that the data analysis from this single-center registry with relatively small numbers of patients was designed to be hypothesis generating in view of the important limitations in drawing conclusions with this kind of study. There are important unadjustable biases that are inevitable in both our PCI and MT groups that are acknowledged.

Conclusion

Among high-risk patients, those ineligible for CABG who are selected for MT may have a predicted mortality in excess of 25% at 1 year. This is more than twice that of those managed with PCI and more marked divergence is seen between outcomes in these groups over time. Coronary complexity has an important relationship with outcomes in CABG-ineligible patients undergoing PCI but not MT. There is also a strong relationship between incomplete revascularization and MACE-free survival. While the causal relationships are yet to be established, the most favorable outcomes in these high-risk patients appear to be seen in those who undergo PCI with complete revascularization.

Compliance with ethical standards

Conflict of interest No conflict of interest to disclose.

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