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Do in-hospital outcomes of isolated coronary artery bypass grafting vary between male and female octogenarians?

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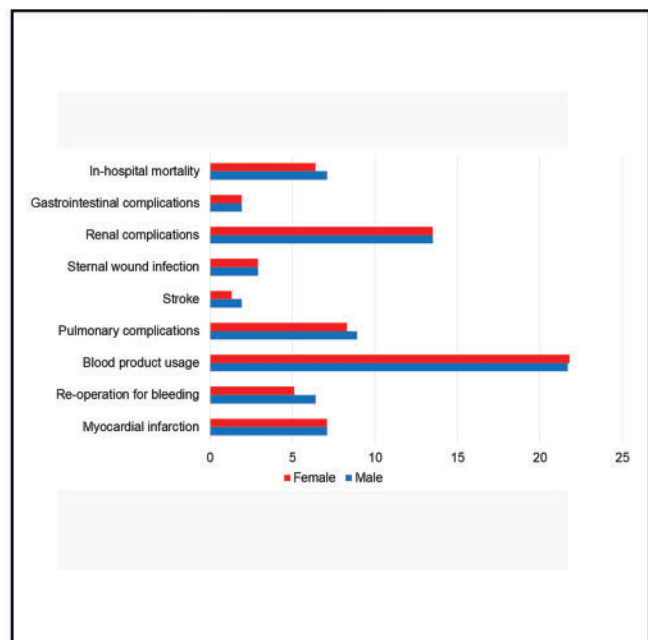
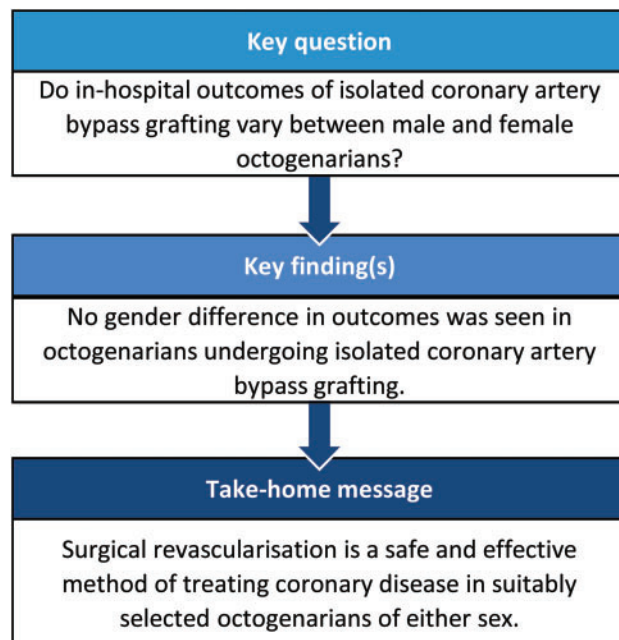
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Abstract

OBJECTIVES: Female gender and advanced age are regarded as independent risk factors for adverse outcomes after isolated coronary artery bypass grafting (CABG). There is paucity of evidence comparing outcomes of CABG between male and female octogenarians. We aimed to analyse in-hospital outcomes of isolated CABG in this cohort.

METHODS: All octogenarians that underwent isolated CABG, from January 2000 to October 2017, were included. A retrospective analysis of a prospectively collected cardiac surgery database (PATS; Dendrite Clinical Systems, Oxford, UK) was performed. A propensity score was generated for each patient from a multivariable logistic regression model based on 25 pre-treatment covariates. A total of 156 matching pairs were derived.

RESULTS: Five hundred and sixty-seven octogenarians underwent isolated CABG. This included 156 females (mean age 82.1 [SD: 0.9]) and 411 males (mean age 82.4 [SD: 2.1 years]). More males were current smokers ($P = 0.002$) with renal impairment ($P = 0.041$), chronic obstructive pulmonary disease ($P = 0.048$), history of cerebrovascular accident ($P = 0.039$) and peripheral vascular disease ($P = 0.027$) while more females had New York Heart Association class 4 ($P = 0.02$), left ventricular ejection fraction 30–49% ($P = 0.038$) and left ventricular ejection fraction $<30\%$ ($P = 0.049$). On-pump, CABG was performed in 140 males and 52 females ($P = 0.921$). There was no difference in in-hospital mortality (5.4% vs 6.4%; $P = 0.840$), stroke (0.9% vs 1.3%; $P = 0.689$), need for renal replacement therapy (17.0% vs 13.5%; $P = 0.732$), pulmonary complications (9.5% vs 8.3%; $P = 0.746$) and sternal wound infection (2.7% vs 2.6%; $P = 0.882$). The outcomes were comparable for the propensity-matched cohorts.

CONCLUSIONS: No gender difference in outcomes was seen in octogenarians undergoing isolated CABG.

Keywords: Coronary artery bypass grafting • Gender • Mortality • Octogenarians • Outcome

ABBREVIATIONS

CABG	Coronary artery bypass grafting
CPB	Cardiopulmonary bypass
ICOR	Index of completeness of revascularization
LIMA	Left internal mammary artery
MIDCAB	Minimally invasive direct coronary artery bypass
PS	Propensity score

INTRODUCTION

It is widely recognized that the female gender is associated with increased perioperative mortality and morbidity after coronary artery bypass grafting (CABG) [1, 2]. Delayed presentation for treatment, delayed recognition of coronary artery disease with increased incidence of acute coronary syndrome, smaller body size with smaller coronary artery size making bypass grafting more challenging as well as increased incidence of comorbidities including diabetes, hypertension and hypercholesterolaemia are some of the plausible explanations for these gender differences in outcomes [3–7].

Advanced age is also a significant predictor of 30-day mortality and postoperative complications after CABG [8, 9]. Octogenarians have several comorbidities such as renal insufficiency, chronic obstructive pulmonary disease, peripheral vascular disease and degenerative cerebral disease that make them high risk for CABG [10]. Despite these comorbidities, a significant number of octogenarians now undergo CABG.

Female gender and advanced age are regarded as independent risk factors for morbidity and mortality after CABG by the 2 most commonly used risk stratification scores, namely EuroSCORE II and STS risk score [11]. Interestingly, gender differences in mortality and morbidity have been predominantly analysed for patients <70 years of age [12]. There is paucity of evidence comparing outcomes of CABG between male and female octogenarians. The aim of our study was to analyse whether or not in-hospital outcomes of isolated CABG vary between male and female octogenarians.

METHODS

Study sample

This study comprised a retrospective analysis of a prospectively collected cardiac surgery database (PATS; Dendrite Clinical Systems, Ltd, Oxford, UK). Because of its retrospective nature,

informed consent was waived for this study. The PATS database captures detailed information on a wide range of preoperative, intraoperative and hospital postoperative variables (including complications and mortality) for all patients undergoing cardiac surgery in our institution. The database was collected and reported in accordance with the Society for Cardiothoracic Surgery in Great Britain and Ireland database criteria. In addition, the medical notes and charts of all the study patients were reviewed.

From January 2000 to October 2017, all male and female octogenarians that underwent isolated first-time CABG at our institution were included in this study. Octogenarians that had reoperative CABG or combined procedures were excluded. The patient characteristics of both groups are shown in Tables 1 and 2. Indications for surgical intervention were determined at a weekly review involving cardiologists, cardiac surgeons and cardiac radiologists. The patients were placed on a specific waiting list according to the urgency of their procedure.

Operative technique

We have previously described our operative technique in detail [10]. Minimally invasive direct coronary artery bypass (MIDCAB) procedure was performed for isolated proximal left anterior descending artery stenosis in all but one case. All MIDCAB procedures were performed through a left anterior small thoracotomy on the beating heart. Patients with multivessel coronary artery disease underwent multivessel CABG. Median sternotomy approach was used for all multivessel CABG. The choice of on- or off-pump strategy was based on the surgeon's preference.

Left internal mammary artery (LIMA) was used for all MIDCAB procedures whereas all patients underwent multivessel CABG using varying combinations of left and/or right internal mammary artery, radial artery and saphenous vein grafts. The choice of conduits was based on the surgeon's preference as well as dictated by patient characteristics. The intraoperative data are summarized in Tables 3 and 4.

Postoperative management

Postoperative intensive care unit management was standardized for all patients. All patients received intravenous nitroglycerine (0.1–8 $\mu\text{g}/\text{kg}/\text{min}$) infusions for the first 24 h unless hypotensive (systolic blood pressure <90 mmHg). Choice of inotropic agents was dictated by the haemodynamic data. Other routine medications included daily aspirin and resumption of cholesterol-lowering agents and beta-blockers unless contraindicated.

Table 1: Comparison of preoperative variables between unmatched female and male octogenarians

Variable	Male (n = 411)	Female (n = 156)	P-value	SMD
Angina (CCS grade 4)	88 (21.4)	35 (22.4)	0.898	0.056
Dyspnoea (NYHA 4)	23 (5.6)	18 (11.5)	0.022*	0.194 ^a
Diabetes	95 (23.1)	35 (22.4)	0.911	0.068
Hypercholesterolaemia	268 (65.2)	101 (64.7)	0.922	0.036
Hypertension	267 (65.0)	98 (62.8)	0.695	0.027
Current smoker	21 (5.1)	0 (0)	0.002*	0.132 ^a
Ex-smoker	198 (48.2)	80 (51.3)	0.792	0.035
Non-smoker	192 (46.7)	76 (48.7)	0.794	0.025
Renal impairment	13 (3.2)	3 (1.9)	0.041*	0.236 ^a
COPD	39 (9.5)	10 (6.4)	0.048*	0.198 ^a
History of CVA	17 (4.1)	4 (2.6)	0.039*	0.242 ^a
PVD	54 (13.1)	15 (9.6)	0.027*	0.296 ^a
Recent MI	80 (19.5)	33 (21.2)	0.862	0.052
Previous PCI	42 (10.2)	16 (10.3)	0.914	0.062
LVEF >50%	318 (77.3)	112 (71.8)	0.068	0.008
LVEF 30–49%	80 (19.5)	35 (22.4)	0.038*	0.244 ^a
LVEF <30%	13 (3.2)	9 (5.8)	0.049*	0.196 ^a
Elective	231 (56.2)	82 (52.6)	0.827	0.009
Urgent	156 (38.0)	64 (41.0)	0.799	0.017
Emergency	24 (5.8)	10 (6.4)	0.843	0.014
Three-vessel disease	290 (70.6)	111 (71.2)	0.892	0.006
Two-vessel disease	98 (23.8)	34 (21.8)	0.896	0.008
One-vessel disease	23 (5.6)	11 (7.1)	0.694	0.015
LMS	154 (37.5)	44 (28.2)	0.499	0.021
Logistic EuroSCORE	6.1 (SD: 2.4)	6.2 (SD: 2.1)	0.867	0.009

*P < 0.05; Values in parentheses are percentages.

^aSMD >0.10 (10%).

CCS: Canadian Cardiovascular Society; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; LMS: left main stem; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease; SD: standard deviation; SMD: standardized mean difference.

Diuretics, angiotensin-converting enzyme inhibitors, other anti-hypertensive agents and oral anticoagulants were gradually introduced when indicated clinically.

Variables and data collection

Preoperative variables of interest included angina (Canadian Cardiovascular Society class), dyspnoea (New York Heart Association class), diabetes, hypercholesterolaemia, hypertension, smoking history, renal insufficiency [preoperative serum creatinine, $\geq 200 \mu\text{M/l}$, moderately impaired renal function (50–85 ml/min), severely impaired renal function (<50 ml/min) off dialysis, and on dialysis], chronic obstructive pulmonary disease (long-term use of bronchodilators or steroids for lung disease), history of cerebrovascular disease, peripheral vascular disease, recent myocardial infarction (within 90 days), previous percutaneous coronary intervention, left ventricular ejection fraction, urgency (operation performed <24 h vs >24 h from time of referral), number of diseased vessels, left main stem and logistic EuroSCORE.

Intraoperative variables of interest included use of cardiopulmonary bypass (CPB), CPB time, aortic cross-clamp time, conversion to CPB, number of grafts, types of grafts used and index of completeness of revascularization (ICOR). The ICOR was defined as the total number of distal grafts constructed divided by the number of the affected coronary vessels reported on the preoperative coronary angiogram [13]. Complete revascularization was assumed when the ICOR was 1 or greater.

Postoperative variables of interest included myocardial infarction (creatinine kinase-MB rise to $>10\times$ the upper reference limit

as a standalone measure or $>5\times$ the upper reference limit with supporting electrocardiographic, angiographic or imaging evidence of myocardial ischaemia), reoperation for bleeding, blood product usage, pulmonary complications (chest infection, reintubation, pneumothorax, pleural effusion, tracheostomy), stroke (transient or permanent), sternal wound infection (superficial or deep), renal complications (acute kidney injury, haemofiltration, dialysis), gastrointestinal complications, length of intensive care unit stay, length of hospital stay and in-hospital mortality.

Ethical statement

All patient identifiable information was removed prior to database analysis. As part of the surgical consent process at our unit all patients consent to the use of their clinical data for research and teaching purposes. As this analysis was performed on retrospective anonymized data, the local ethics committee advised us that any further ethical approval was not required.

Statistical analysis

Statistical analysis was performed using the SAS for Windows version 9.3 (SAS, Cary, NC USA). The summary results for numeric variables were presented as mean (SD). The summary results for categorical variables were presented as frequency and percentage. The Chi-squared test was used to compare the categorical variables. The numeric variables were tested for normality, and the Mann-Whitney U-test or the 2-tailed, independent-samples

Table 2: Comparison of preoperative variables between matched female and male octogenarians

Variable	Male (n = 156)	Female (n = 156)	P-value	SMD
Angina (CCS grade 4)	38 (24.4)	35 (22.4)	0.934	0.032
Dyspnoea (NYHA 4)	15 (9.6)	18 (11.5)	0.918	0.072
Diabetes	39 (25.0)	35 (22.4)	0.929	0.071
Hypercholesterolaemia	107 (68.6)	101 (64.7)	0.976	0.032
Hypertension	103 (66.0)	98 (62.8)	0.914	0.029
Current smoker	1 (0.6)	0 (0)	0.224	0.068
Ex-smoker	82 (52.6)	80 (51.3)	0.886	0.041
Non-smoker	79 (50.6)	76 (48.7)	0.784	0.032
Renal impairment	4 (2.6)	3 (1.9)	0.187	0.096
COPD	13 (8.3)	10 (6.4)	0.321	0.089
History of CVA	5 (3.2)	4 (2.6)	0.292	0.092
PVD	17 (10.9)	15 (9.6)	0.876	0.099
Recent MI	33 (21.2)	33 (21.2)	1.00	0.010
Previous PCI	17 (10.9)	16 (10.3)	0.963	0.012
LVEF >50%	127 (81.4)	112 (71.8)	0.356	0.021
LVEF 30–49%	29 (18.6)	35 (22.4)	0.795	0.091
LVEF <30%	8 (5.1)	9 (5.8)	0.789	0.067
Elective	85 (54.5)	82 (52.6)	0.782	0.008
Urgent	60 (38.5)	64 (41.0)	0.824	0.018
Emergency	11 (7.0)	10 (6.4)	0.899	0.019
Three-vessel disease	113 (72.4)	111 (71.2)	0.772	0.007
Two-vessel disease	33 (21.2)	34 (21.8)	0.992	0.009
One-vessel disease	10 (6.4)	11 (7.1)	0.882	0.013
LMS	48 (30.8)	44 (28.2)	0.784	0.037
Logistic EuroSCORE	6.1 (SD: 1.7)	6.2 (SD: 2.1)	0.918	0.007

Values in parentheses are percentages.

CCS: Canadian Cardiovascular Society; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; LMS: left main stem; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease; SD: standard deviation; SMD: standardized mean difference.

Table 3: Comparison of intraoperative variables between unmatched female and male octogenarians

Variable	Male (n = 411)	Female (n = 156)	P-value	SMD
CPB	140 (34.1)	52 (33.3)	0.921	0.036
OPCAB	271 (65.9)	104 (66.7)	0.972	0.042
CPB time	94.1 (SD: 54.6)	93.4 (SD: 52.9)	0.754	0.061
Aortic cross-clamp time	52.7 (SD: 29.8)	51.9 (SD: 28.1)	0.798	0.062
Conversion to CPB	3 (1.1)	1 (0.9)	0.990	0.029
Three or more grafts	238 (57.9)	75 (48.1)	0.038*	0.218 ^a
Two grafts	151 (36.7)	70 (44.9)	0.056	0.031
One graft	22 (5.4)	11 (7.0)	0.289	0.078
MIDCAB	22 (5.4)	11 (7.0)	0.289	0.078
LIMA only	22 (5.4)	11 (7.0)	0.289	0.078
LIMA + SVG	312 (75.9)	128 (82.1)	0.587	0.042
LIMA + Radial	7 (1.7)	3 (1.9)	0.898	0.012
LIMA + Radial + SVG	3 (0.7)	1 (0.6)	0.992	0.010
BIMA only	22 (5.4)	4 (2.6)	0.041*	0.192 ^a
BIMA + SVG	25 (6.1)	5 (3.2)	0.027*	0.242 ^a
BIMA + Radial	13 (3.2)	3 (1.9)	0.068	0.041
BIMA + Radial + SVG	7 (1.7)	1 (0.6)	0.089	0.072
ICOR	1.16 (SD: 0.22)	1.15 (SD: 0.07)	0.792	0.068

*P < 0.05; Values in parentheses are percentages.

^aSMD > 0.10 (10%).

BIMA: bilateral internal mammary arteries; CPB: cardiopulmonary bypass; ICOR: index of completeness of revascularization; LIMA: left internal mammary artery; OPCAB: off-pump coronary artery bypass; MIDCAB: minimally invasive direct coronary artery bypass; SD: standard deviation; SMD: standardized mean difference; SVG: saphenous vein graft.

Student's *t*-test was used accordingly. Statistical significance was defined as *P* < 0.05.

Propensity score (PS) matching was used to reduce the effect of gender-selection bias. PS was estimated by

multivariable logistic regression analysis with a binary dependent variable representing female versus male. Independent variables included all the preoperative variables (Table 1). Patients were 1:1 matched on the logit of the PS using a

Table 4: Comparison of intraoperative variables between matched female and male octogenarians

Variable	Male (n = 156)	Female (n = 156)	P-value	SMD
CPB	54 (34.6)	52 (33.3)	0.762	0.054
OPCAB	102 (65.4)	104 (66.7)	0.954	0.029
CPB time	93.7 (SD: 53.1)	93.4 (SD: 52.9)	0.889	0.031
Aortic cross-clamp time	52.1 (SD: 28.3)	51.9 (SD: 28.1)	0.992	0.011
Conversion to CPB	1 (0.9)	1 (0.9)	1.00	0.009
Three or more grafts	81 (51.9)	75 (48.1)	0.789	0.042
Two grafts	65 (41.7)	70 (44.9)	0.684	0.062
One graft	10 (6.4)	11 (7.0)	0.862	0.034
MIDCAB	10 (6.4)	11 (7.0)	0.862	0.034
LIMA only	10 (6.4)	11 (7.0)	0.862	0.034
LIMA + SVG	127 (81.4)	128 (82.1)	0.776	0.048
LIMA + Radial	4 (2.6)	3 (1.9)	0.798	0.040
LIMA + Radial + SVG	2 (1.3)	1 (0.6)	0.882	0.033
BIMA only	3 (1.9)	4 (2.6)	0.756	0.039
BIMA + SVG	5 (3.2)	5 (3.2)	1.00	0.009
BIMA + Radial	3 (1.9)	3 (1.9)	1.00	0.009
BIMA + Radial + SVG	2 (1.3)	1 (0.6)	0.452	0.074
ICOR	1.16 (SD: 0.19)	1.15 (SD: 0.07)	0.824	0.033

Values in parentheses are percentages.

BIMA: bilateral internal mammary arteries; CPB: cardiopulmonary bypass; ICOR: index of completeness of revascularization; LIMA: left internal mammary artery; OPCAB: off-pump coronary artery bypass; MIDCAB: minimally invasive direct coronary artery bypass; SD: standard deviation; SMD: standardized mean difference; SVG: saphenous vein graft.

calliper of width equal to 0.25 standard deviation of the logit of PS.

To detect imbalances in baseline covariates, standardized mean differences were used. Standardized mean differences represent the difference in means between the 2 groups in units of standard deviation. They do not depend on the unit of measurement and are not influenced by sample size. Standardized mean differences of <0.10 (10%) are likely to indicate a negligible imbalance between the 2 groups. Paired-samples *t*-test and McNemar's test were used for comparison of propensity-matched groups.

RESULTS

During the study period, 567 octogenarians underwent isolated first-time CABG. The study cohort included 156 females (mean age 82.1 [SD: 0.9]) and 411 males (mean age 82.4 [SD: 2.1 years]). The 2 groups were comparable for 17 of the 25 pre-treatment variables (Table 1).

Females represented 27.5% of the study cohort. They had a higher prevalence of New York Heart Association class 4 ($P=0.02$), left ventricular ejection fraction 30–49% ($P=0.038$) and left ventricular ejection fraction <30% ($P=0.049$). On the other hand, more males were current smokers ($P=0.002$) with renal impairment ($P=0.041$), chronic obstructive pulmonary disease ($P=0.048$), history of cerebrovascular accident ($P=0.039$) and peripheral vascular disease ($P=0.027$). The preoperative variables for the matched cohorts are summarized in Table 2. After matching, treated patients were similar with regards to all baseline covariates used for PS estimation. Matching reduced covariate imbalance and improved covariate balance across treatment groups.

A total of 33 MIDCAB procedures and 534 multivessel CABG were performed for the entire cohort during the study period. Off-pump CABG was the predominant surgical revascularization

strategy with 66.1% of the procedures performed without CPB. There was no gender disparity in the use of LIMA with 100% use in both groups. However, more male patients received bilateral internal mammary arteries only ($P=0.041$) and bilateral internal mammary arteries with supplemental saphenous vein grafts ($P=0.027$). Despite, differences in the use of bilateral internal mammary arteries, the ICOR for male and female cohorts was similar (1.16 [SD: 0.22] vs 1.15 [SD: 0.07]; $P=0.792$). Intraoperative data are summarized in Table 3 for unmatched cohorts.

Table 5 summarizes the comparison of key in-hospital postoperative outcomes for unmatched cohorts. Both groups reported similar outcomes except for the rate of renal complications. The rate of renal complications (including use of haemofiltration) was higher for males although the difference failed to reach statistical significance ($P=0.052$). There was no mortality in the MIDCAB cohort.

Matching on estimated PS made available a matched cohort of 312 patients, including 156 patients in each group with similar demographic, clinical and angiographic risk profiles (Table 2). The intraoperative variables (Table 4) and the postoperative outcomes (Table 6) were comparable for the propensity-matched cohorts as well (Figure 1).

DISCUSSION

The key findings of this study are that in-hospital outcomes of isolated CABG do not vary between unmatched and matched male and female octogenarians.

Gender differences in outcomes of CABG remain a contentious issue. However, a large volume of published evidence reports female gender as a well-established risk factor for increased postoperative morbidity and mortality after isolated CABG [1, 2]. Interestingly, most studies reporting female gender as an independent risk factor for poor outcomes after CABG analysed patients <70 years of age [12] with a paucity of evidence

Table 5: Comparison of postoperative outcomes between unmatched male and female octogenarians

Outcome	Male (n = 411)	Female (n = 156)	P-value
Myocardial infarction	27 (6.6)	11 (7.1)	0.548
Reoperation for bleeding	24 (5.8)	8 (5.1)	0.841
Blood product usage	98 (23.8)	34 (21.8)	0.879
Pulmonary complications	39 (9.5)	13 (8.3)	0.746
Stroke (transient)	6 (1.5)	0 (0)	0.195
Stroke (permanent)	4 (0.9)	2 (1.3)	0.689
Sternal wound infection ^a	11 (2.8)	4 (2.8)	1.00
Renal complications	70 (17.0)	21 (13.5)	0.052
Gastrointestinal complications	6 (1.5)	3 (1.9)	0.832
ICU length of stay (days)	1.9 (SD: 0.4)	1.9 (SD: 0.1)	0.891
Hospital length of stay (days)	12.7 (SD: 4.2)	12.9 (SD: 4.7)	0.776
In-hospital mortality	22 (5.4)	10 (6.4)	0.840

Values in parentheses are percentages.

^aMIDCAB cases excluded from total number of cases for calculation of rate of sternal wound infection.

ICU: intensive care unit; MIDCAB: minimally invasive direct coronary artery bypass; SD: standard deviation.

Table 6: Comparison of postoperative outcomes between matched male and female octogenarians

Outcome	Male (n = 156)	Female (n = 156)	P-value
Myocardial infarction	11 (7.1)	11 (7.1)	1.00
Reoperation for bleeding	10 (6.4)	8 (5.1)	0.917
Blood product usage	89 (21.7)	34 (21.8)	0.992
Pulmonary complications	14 (8.9)	13 (8.3)	0.922
Stroke (transient)	1 (0.6)	0 (0)	0.897
Stroke (permanent)	2 (1.3)	2 (1.3)	1.00
Sternal wound infection ^a	4 (2.9)	4 (2.9)	1.00
Renal complications	21 (13.5)	21 (13.5)	1.00
Gastrointestinal complications	3 (1.9)	3 (1.9)	1.00
ICU length of stay (days)	1.9 (SD: 0.2)	1.9 (SD: 0.1)	0.992
Hospital length of stay (days)	12.7 (SD: 4.5)	12.9 (SD: 4.7)	0.892
In-hospital mortality	11 (7.1)	10 (6.4)	0.779

Values in parentheses are percentages.

^aMIDCAB cases excluded from total number of cases for calculation of rate of sternal wound infection.

ICU: intensive care unit; MIDCAB: minimally invasive direct coronary artery bypass; SD: standard deviation.

comparing outcomes of CABG between male and female octogenarians. In one of the largest studies published to date of 24 461 patients of age ≥ 80 years who underwent bypass surgery from 1987 through 1990, Peterson *et al.* [14] reported female gender as a predictor of adverse outcomes. On the contrary, in a recently published single-centre study of all patients over 60 years of age undergoing isolated CABG during 2001 and 2011, categorized by age into sexagenarians (2266, 16.6% women), septuagenarians (2332, 25.4% women) and octogenarians (374, 32% women), Arif *et al.* investigated possible gender-related differences in outcome after CABG divided into age by decades. For their octogenarian cohort, they did not see gender disparity. The results of our study are similar to those reported by Arif *et al.* [12].

We attribute this lack of gender differences in outcomes for our cohort to extensive use of off-pump revascularization strategy, aggressive use of LIMA and adherence to complete revascularization as reflected by similar ICOR for the 2 cohorts. There is evidence to suggest that off-pump CABG disproportionately benefits women and narrows the gender disparity in outcomes [15, 16]. Off-pump CABG attenuates the inflammatory response associated with CPB and preserves organ function [17]. This benefit is more pronounced for high-risk cohorts of patients including women and octogenarians [10, 15, 16, 18]. In addition, off-pump CABG reduces haemodilution and transfusion requirements which has a beneficial impact on patients with small body surface area particularly females [19]. Traditionally, females undergoing CABG have received fewer bypass grafts with underutilization of LIMA [20]. There is evidence to suggest that complete revascularization with aggressive use of arterial grafts particularly LIMA for grafting the left anterior descending artery improves outcomes in octogenarians [21]. We believe that 100% LIMA usage with similar ICOR reflecting completeness of revascularization could also account for comparable outcomes for male and female octogenarians in our study.

One of the criticisms of our study is the high mortality rate of our octogenarian cohort. However, overall mortality rate of 5.6% for our cohort is better than that reported by Arif *et al.* [12] (11.2%), Peterson *et al.* [14] (11.1%), Scott *et al.* [22] (9.0%) and comparable to the 5.1% reported by Bardacki *et al.* [23].

Importantly, our institutional mortality has continued to decline over the years (Table 7). This improvement is a reflection of the concomitant improvement in preoperative optimization of this high-risk cohort as well as the advances in anaesthetic management, surgical techniques and technology as well as postoperative care and rehabilitation. Similarly, there has been a remarkable improvement in length of hospital stay from nearly 12.5 days to around 7 days over the last 17 years. The discharge of octogenarians to home is a complex process. The presence of comorbid conditions, social circumstances, delayed healing and enhanced predisposition to postoperative complications are some of the key determinants of length of hospital stay [23]. Attention to modifiable factors, creation of a discharge support service and establishment of an active postoperative rehabilitation programme are some of the interventions that have enabled us to reduce the length of stay for octogenarians in our institution.

After cardiac surgery, acute kidney injury of varying severity occurs in up to one-third of all patients and approximately 2% require temporary renal replacement therapy [24]. Elderly patients are at a much increased risk of developing this complication. The pathogenesis of acute renal insult after cardiac surgery is multifactorial and may develop from a combination of impaired autoregulation caused by comorbidities and drugs, affected renal perfusion due to altered haemodynamics during the operation and in the perioperative period, and the procedure-induced systemic inflammatory response [25]. The rate of renal complications of 16% including the use of renal replacement therapy for our cohort is better than that reported by other authors [25, 26]. We attribute this relatively low rate of renal complications to possible case selection as well as active identification of high-risk patients for renal complications, optimization of renal perfusion and avoidance of nephrotoxins.

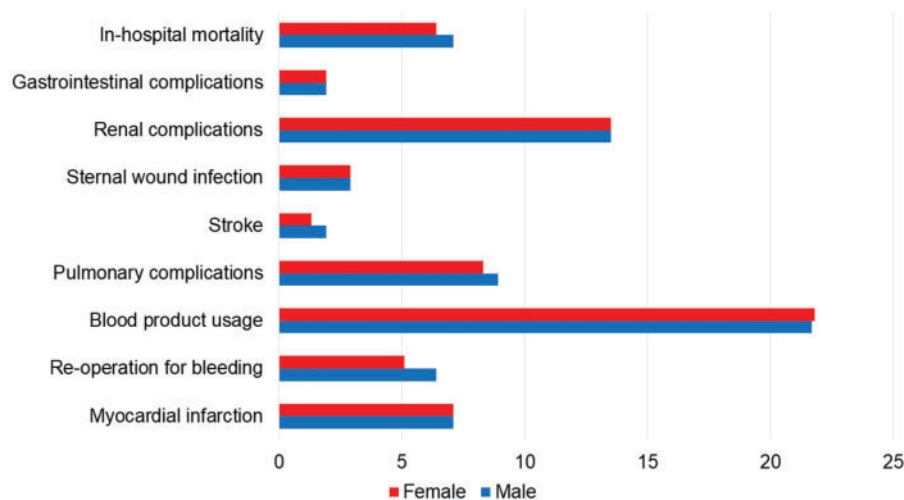
Limitations

Our study has all the limitations attributed to a single-centre, retrospective analysis. We used PS matching to address differences

Table 7: Yearly isolated CABG and in-hospital mortality rate for male and female octogenarians

Year	Male CABG	Male death	In-hospital mortality rate (%)	Female CABG	Female death	In-hospital mortality rate (%)
2000	13	2	15.4	7	2	28.6
2001	18	3	16.7	5	0	0
2002	18	2	11.1	8	1	12.5
2003	13	0	0	9	2	22.2
2004	22	1	4.5	5	0	0
2005	16	0	0	4	0	0
2006	14	1	7.1	8	0	0
2007	19	2	10.5	5	1	20
2008	26	3	11.5	10	0	0
2009	29	0	0	10	1	10
2010	37	3	8.1	16	1	6.3
2011	33	1	3.0	12	1	8.3
2012	16	0	0	10	0	0
2013	30	2	6.7	8	0	0
2014	21	1	4.8	12	0	0
2015	30	0	0	12	1	8.3
2016	30	1	3.3	10	0	0
2017	26	0	0	5	0	0

CABG: coronary artery bypass grafting.

**Figure 1:** Comparison of postoperative outcomes for propensity-matched cohorts.

in risk profiles of the 2 groups. However, outcomes are multifactorial and also influenced by unmeasured confounders and hidden biases that may have affected our results. Furthermore, lack of angiographic assessment of graft patency and information about the cause of death are additional limitations of this analysis. Most importantly, the study spans a period of 17 years. This is both a strength of the paper as well as a very important confounder. During this period, several surgeons operated on these patients and their techniques and outcomes may have differed besides having a temporal relationship with outcome. Similarly, off-pump coronary artery bypass and MIDCAB have been more commonly utilized in the latter period of the study and at least in the initial part of the study a selection bias regarding cases taken up for off-pump coronary artery bypass cannot be excluded. One could argue that there is a need for a randomized multi-centre trial to provide robust evidence to address this controversial issue. However, such a trial will be difficult to conduct as calculation of sample size can be a complex issue impacted by

the choice of primary endpoint as well as the occurrence rate of chosen endpoint at the participating centres. The sample size will vary significantly depending on whether death alone or a composite of death or a major adverse event (myocardial infarction, stroke, acute renal failure requiring renal replacement therapy or repeat revascularization) within 30 days is chosen as the primary endpoint. In addition, whether the trial will use an 'all comers' approach or will have strict selection criteria may determine if the results will be representative for a large and well-defined patient population.

CONCLUSION

No gender difference in outcomes was seen in octogenarians undergoing isolated CABG in this single-centre study.

Conflict of interest: none declared.

Data Availability Statement

All patient confidential data are stored in the cardiac surgery database (PATS; Dendrite Clinical Systems, Ltd, Oxford, UK) at Harefield Hospital. All relevant meta-data are within the manuscript and its Supporting Information files.

Author contributions

Rizwan Q. Attia: Methodology; Writing—original draft; Writing—review & editing. **Eve Katumalla:** Data curation; Methodology. **Shabnam Cyclewala:** Data curation; Formal analysis. **Melissa Rochon:** Data curation; Formal analysis; Investigation. **Nandor Marczin:** Conceptualization; Investigation; Supervision; Visualization; Writing—original draft. **Shahzad G. Raja:** Conceptualization; Formal analysis; Investigation; Project administration; Supervision; Validation; Writing—original draft; Writing—review & editing.

Reviewer information

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