Preoperative thrombolysis	1	11%	11%	Active MI	1	8%	8%	8%
Total variables (excl. combinations)	31			Diffuse/severe disease	1	8%	8%	8%
				Type of graft(s)	1	8%	8%	-25%
				Comb. HTN or BP	1	8%	8%	-3%
				Inotropic medication	1	8%	8%	8%
				Comb. critical state	1	8%	8%	8%
				Comb. PCI variables	1	8%	8%	8%
				Total variables (excl. combinations)	35			

Δa: change from < 1998; Δb: change from 1998-2007. Comb: combination variable; CHF: congestive heart failure; NYHA: New York Heart Association; MI: myocardial infarction; ECG: electrocardiogram; IABP: intra-aortic baloon pump; HTN: hypertension; BP: blood pressure; PCI: percutaneous coronary intervention; PTCA: percutaneous transluminal coronary angioplasty; CPR: cardiopulmonary resuscitation; ASA: American Society of Anethesiology; ACE: angiotensin converting enzyme; INR: international normalized ratio; PT: prothromin time

Table 5. Models containing only preoperative data

All models			**Short-term models**			**Long-term models**		
Variable	***n* = 89**	**%**	**Variable**	***n*= 75**	**%**	**Variable**	***n* = 14**	**%**
Age	79	89%	Age	68	91%	Age	11	79%
Left ventricular function	62	70%	Left ventricular function	52	69%	Renal failure	11	79%
Renal failure	54	61%	Urgency	46	61%	Left ventricular function	10	71%
Comb. arterial disease	52	58%	Gender	45	60%	Diabetes	9	64%
Comb. heart failure variables	52	58%	Repeat operation	44	59%	Comb. arterial disease	9	64%
Gender	51	57%	Renal failure	43	57%	Comb. heart failure variables	9	64%
Urgency	50	56%	Comb. arterial disease	43	57%	Peripheral arterial disease	8	57%
Repeat operation	48	54%	Comb. heart failure variables	43	57%	Comb. CHF or NYHA	8	57%
Peripheral arterial disease	45	51%	History of MI	38	51%	Lung disease	7	50%
Comb. CHF or NYHA	44	49%	Comb. any MI variable	38	51%	Gender	6	43%
History of MI	42	47%	Peripheral arterial disease	37	49%	Neurologic disease	6	43%
Comb. any MI variable	42	47%	Comb. CHF or NYHA	36	48%	Comb. vessel disease	6	43%
Lung disease	41	46%	Comb. critical state	36	48%	Body size measurements	5	36%
Comb. critical state	40	45%	Lung disease	34	45%	Congestive heart failure	5	36%
Diabetes	37	42%	Comb. vessel disease	31	41%	Left main disease	5	36%
Comb. vessel disease	37	42%	Diabetes	28	37%	Urgency	4	29%
Neurologic disease	32	36%	Neurologic disease	26	35%	Repeat operation	4	29%
Left main disease	28	31%	Left main disease	23	31%	History of MI	4	29%
Congestive heart failure	27	30%	Cardiogenic shock	23	31%	Comb. any MI variable	4	29%
Cardiogenic shock	27	30%	Congestive heart failure	22	29%	Hypertension	4	29%
Body size measurements	26	29%	Body size measurements	21	28%	Comb. HTN or BP	4	29%
Number of diseased vessels	23	26%	Number of diseased vessels	20	27%	Race or ethnicity	4	29%
NYHA class	21	24%	NYHA class	18	24%	Comb. critical state	4	29%
Hypertension	19	21%	Comb. ECG or arrhythmia variables	17	23%	Smoking status	4	29%
Comb. HTN or BP	19	21%	Hypertension	15	20%	Cardiogenic shock	4	29%
Comb. ECG or arrhythmia variables	19	21%	Comb. HTN or BP	15	20%	NYHA class	3	21%

Angina	18	20%
Comb. PCI variables	18	20%
Valve disease	16	18%
Preoperative IABP use	15	17%
Prior/recent PCI or PTCA	14	16%
Inotropic medication	13	15%
Any arrhythmia	12	13%
Pulmonary hypertension	10	11%
Race or ethnicity	10	11%
Preoperative diuretic use	8	9%
Nitroglycerin use	8	9%
Smoking status	8	9%
Atrial arrhythmia	8	9%
Extracardiac arteriopathy	7	8%
Liver disease	7	8%
Cardiomegaly	7	8%
Immunosuppression	7	8%
Diffuse/severe disease	5	6%
Digoxin or digitalis use	5	6%
Dyspnea	4	4%
Pulmonary rales	4	4%
Date or order of surgery	4	4%
On- *vs.* off-pump CABG	4	4%
Ventricular or unstable arrhythmia	4	4%
Critical state	4	4%
Ventricular wall motion	3	3%
PTCA failure/emergency	3	3%
Hypercholesterolemia	3	3%
Anticoagulation or antiplatelet use	3	3%
Anemia (hemoglobin, hematocrit)	3	3%
A published comorbidity index	3	3%
Other preoperative labs	3	3%
Cachexia or malnutrition	2	2%
Type of MI	2	2%
Active MI	2	2%
Preoperative CPR/cardiac arrest	2	2%
Endocarditis	2	2%
Stent thrombosis	2	2%
Other ECG abnormalities	2	2%
Disaster, catastrophic state	2	2%
Preop intubation	2	2%

Angina	15	20%
Comb. PCI variables	15	20%
Valve disease	13	17%
Preoperative IABP use	12	16%
Prior/recent PCI or PTCA	11	15%
Any arrhythmia	11	15%
Inotropic medication	10	13%
Pulmonary hypertension	10	13%
Nitroglycerin use	8	11%
Preoperative diuretic use	7	9%
Cardiomegaly	7	9%
Race or ethnicity	6	8%
Extracardiac arteriopathy	6	8%
Liver disease	6	8%
Atrial arrhythmia	5	7%
Smoking status	4	5%
Immunosuppression	4	5%
Diffuse/severe disease	4	5%
Digoxin or digitalis use	4	5%
Dyspnea	4	5%
Pulmonary rales	4	5%
Critical state	4	5%
On- *vs.* off-pump CABG	3	4%
Ventricular or unstable arrhythmia	3	4%
Ventricular wall motion	3	4%
PTCA failure/emergency	3	4%
Anticoagulation or antiplatelet use	3	4%
Anemia (hemoglobin, hematocrit)	3	4%
A published comorbidity index	3	4%
Other preoperative labs	3	4%
Hypercholesterolemia	2	3%
Cachexia or malnutrition	2	3%
Type of MI	2	3%
Active MI	2	3%
Preoperative CPR/cardiac arrest	2	3%
Endocarditis	2	3%
Stent thrombosis	2	3%
Other ECG abnormalities	2	3%
Disaster, catastrophic state	2	3%
Preop intubation	2	3%
Steroid use	2	3%

Angina	3	21%
Number of diseased vessels	3	21%
Valve disease	3	21%
Preoperative IABP use	3	21%
Inotropic medication	3	21%
Immunosuppression	3	21%
Date or order of surgery	3	21%
Prior/recent PCI or PTCA	3	21%
Comb. PCI variables	3	21%
Atrial arrhythmia	3	21%
Comb. ECG or arrhythmia variables	2	14%
Extracardiac arteriopathy	1	7%
Preoperative diuretic use	1	7%
Diffuse/severe disease	1	7%
Liver disease	1	7%
On- *vs.* off-pump CABG	1	7%
Any arrhythmia	1	7%
Ventricular or unstable arrhythmia	1	7%
Hypercholesterolemia	1	7%
Digoxin or digitalis use	1	7%
Functional state	1	7%
Recent admissions	1	7%
Cachexia or malnutrition	0	0%
Ventricular wall motion	0	0%
Pulmonary hypertension	0	0%
Calcified aorta	0	0%
Dyspnea	0	0%
Type of MI	0	0%
Active MI	0	0%
Pulmonary rales	0	0%
Killip classification	0	0%
Number of grafts	0	0%
Type of graft(s)	0	0%
Comb. graft variables	0	0%
Blood pressure	0	0%
Nitroglycerin use	0	0%
Cardiopulmonary bypass time	0	0%
Cardiomegaly	0	0%
Preoperative CPR/cardiac arrest	0	0%
Location or type of surgical center	0	0%
Center's case frequency	0	0%

Steroid use	2	2%	Preoperative cardiac biomarkers	2	3%	Aortic cross-clamp duration	0	0%
Preoperative cardiac biomarkers	2	2%	Date or order of surgery	1	1%	Endocarditis	0	0%
Recent admissions	2	2%	Recent admissions	1	1%	Abdominal aortic aneurysm	0	0%
Calcified aorta	1	1%	Calcified aorta	1	1%	PTCA failure/emergency	0	0%
Killip classification	1	1%	Killip classification	1	1%	Stent thrombosis	0	0%
Location or type of surgical center	1	1%	Location or type of surgical center	1	1%	Any family history variable	0	0%
Any family history variable	1	1%	Any family history variable	1	1%	Antiarrhythmic agents	0	0%
Antiarrhythmic agents	1	1%	Antiarrhythmic agents	1	1%	Other ECG abnormalities	0	0%
Non-CABG surgery	1	1%	Non-CABG surgery	1	1%	Non-CABG surgery	0	0%
Preoperative thrombolysis	1	1%	Preoperative thrombolysis	1	1%	Anticoagulation or antiplatelet use	0	0%
PT or INR	1	1%	PT or INR	1	1%	Preoperative thrombolysis	0	0%
Transfusion	1	1%	Transfusion	1	1%	PT or INR	0	0%
Serum albumin	1	1%	Serum albumin	1	1%	Critical state	0	0%
ACE inhibitor use	1	1%	ACE inhibitor use	1	1%	Disaster, catastrophic state	0	0%
Functional state	1	1%	ASA classification	1	1%	Anemia (hemoglobin, hematocrit)	0	0%
ASA classification	1	1%	Insurance type or status	1	1%	Transfusion	0	0%
Insurance type or status	1	1%	Acute mental status changes	1	1%	Refused blood products	0	0%
Acute mental status changes	1	1%	Functional state	0	0%	Preop intubation	0	0%
Number of grafts	0	0%	Number of grafts	0	0%	Concurrent procedure	0	0%
Type of graft(s)	0	0%	Type of graft(s)	0	0%	A published comorbidity index	0	0%
Comb. graft variables	0	0%	Comb. graft variables	0	0%	Heart rate	0	0%
Blood pressure	0	0%	Blood pressure	0	0%	Steroid use	0	0%
Cardiopulmonary bypass time	0	0%	Cardiopulmonary bypass time	0	0%	Preoperative cardiac biomarkers	0	0%
Center's case frequency	0	0%	Center's case frequency	0	0%	Other preoperative labs	0	0%
Aortic cross-clamp duration	0	0%	Aortic cross-clamp duration	0	0%	Serum albumin	0	0%
Abdominal aortic aneurysm	0	0%	Abdominal aortic aneurysm	0	0%	Other preoperative comorbidities	0	0%
Refused blood products	0	0%	Refused blood products	0	0%	ACE inhibitor use	0	0%
Concurrent procedure	0	0%	Concurrent procedure	0	0%	Patient education level/literacy	0	0%
Heart rate	0	0%	Heart rate	0	0%	ASA classification	0	0%
Other preoperative comorbidities	0	0%	Other preoperative comorbidities	0	0%	Insurance type or status	0	0%
Patient education level/literacy	0	0%	Patient education level/literacy	0	0%	Left ventricular hypertrophy	0	0%
Left ventricular hypertrophy	0	0%	Left ventricular hypertrophy	0	0%	Time from admission to procedure	0	0%
Time from admission to procedure	0	0%	Time from admission to procedure	0	0%	Acute mental status changes	0	0%
Intraoperative variables	0	0%	Intraoperative variables	0	0%	Intraoperative variables	0	0%
Postoperative variables	0	0%	Postoperative variables	0	0%	Postoperative variables	0	0%
Total variables (excl. combinations)	76		Total variables (excl. combinations)	75		Total variables (excl. combinations)	39	

Comb: combination variable; CHF: congestive heart failure; NYHA: New York Heart Association; MI: myocardial infarction; ECG: electrocardiogram; IABP: intra-aortic baloon pump; HTN: hypertension; BP: blood pressure; PCI: percutaneous coronary intervention; PTCA: percutaneous transluminal coronary angioplasty; CPR: cardiopulmonary resuscitation; ASA: American Society of Anethesiology; ACE: angiotensin converting enzyme; INR: international normalized ratio; PT: prothromin time

Table 6. Models considering on- *vs.* off- pump CABG

All models			Short-term models			Long-term models		
Variable	***n* = 4**	**%**	**Variable**	***n* = 3**	**%**	**Variable**	***n* = 1**	**%**
Age	4	100%	Age	3	100%	Age	1	100%
On- *vs.* off-pump CABG	4	100%	On- *vs.* off-pump CABG	3	100%	History of MI	1	100%
Gender	2	50%	Gender	2	67%	Comb. any MI variable	1	100%
Renal failure	2	50%	Renal failure	2	67%	On- *vs.* off-pump CABG	1	100%
Urgency	2	50%	Urgency	2	67%	Total variables (excl. combinations)	3	
History of MI	2	50%	Comb. critical state	2	67%			
Comb. any MI variable	2	50%	Body size measurements	1	33%			
Comb. critical state	2	50%	Diabetes	1	33%			
Body size measurements	1	25%	Left ventricular function	1	33%			
Diabetes	1	25%	Lung disease	1	33%			
Left ventricular function	1	25%	Pulmonary hypertension	1	33%			
Lung disease	1	25%	Repeat operation	1	33%			
Pulmonary hypertension	1	25%	Neurologic disease	1	33%			
Repeat operation	1	25%	Peripheral arterial disease	1	33%			
Neurologic disease	1	25%	Comb. arterial disease	1	33%			
Peripheral arterial disease	1	25%	NYHA class	1	33%			
Comb. arterial disease	1	25%	History of MI	1	33%			
NYHA class	1	25%	Active MI	1	33%			
Active MI	1	25%	Comb. any MI variable	1	33%			
Preoperative diuretic use	1	25%	Preoperative diuretic use	1	33%			
Comb. heart failure variables	1	25%	Comb. heart failure variables	1	33%			
Comb. CHF or NYHA	1	25%	Comb. CHF or NYHA	1	33%			
Number of diseased vessels	1	25%	Number of diseased vessels	1	33%			
Comb. vessel disease	1	25%	Comb. vessel disease	1	33%			
Hypertension	1	25%	Hypertension	1	33%			
Comb. HTN or BP	1	25%	Comb. HTN or BP	1	33%			
Race or ethnicity	1	25%	Race or ethnicity	1	33%			
Preoperative IABP use	1	25%	Preoperative IABP use	1	33%			
Inotropic medication	1	25%	Inotropic medication	1	33%			
Left main disease	1	25%	Left main disease	1	33%			
Cardiogenic shock	1	25%	Cardiogenic shock	1	33%			
Any arrhythmia	1	25%	Any arrhythmia	1	33%			
Comb. ECG or arrhythmia variables	1	25%	Comb. ECG or arrhythmia variables	1	33%			
Steroid use	1	25%	Steroid use	1	33%			
Total variables (excl. combinations)	26		Total variables (excl. combinations)	26				

Comb: combination variable; CHF: congestive heart failure; NYHA: New York Heart Association; MI: myocardial infarction; ECG: electrocardiogram; IABP: intra-aortic baloon pump; HTN: hypertension; BP: blood pressure; PCI: percutaneous coronary intervention; PTCA: percutaneous transluminal coronary angioplasty; CPR: cardiopulmonary resuscitation; ASA: American Society of Anethesiology; ACE: angiotensin converting enzyme; INR: international normalized ratio; PT: prothromin time

minor differences in the pre-CABG patients' risk factor frequency (which may have been associated with provider-based off-pump patient selection criteria), the pre-CABG patient risk factors identified were extremely similar to the overall findings, as reported above. Given the smaller number of on-pump *vs.* off-pump CABG mortality risk model comparisons reported, however, these findings may have limited generalizability.

When reviewing the frequency distribution of preoperative model risk variables, it is striking how very few modifiable (as opposed to non-modifiable) patient risk factors have been identified with a post-CABG mortality impact. As an inherently non-modifiable risk factor, the risk for post-CABG mortality increases as a patient's age increases. Perhaps by the time a patient is being evaluated for a CABG procedure, the negative prognostic impact for the most common preoperative risk factors, such as diabetes mellitus and poor left ventricular ejection fraction, may be difficult to reverse or otherwise counteract in the ST; however, these impacts can be seen in LT models.

In contrast, several of these reported patient risk factors have potential to be mitigated. As an example, body mass index or another marker of body habitus (e.g., height, weight, or body surface area) was included in 31/133 (23%) of ST models considering only preoperative risk factors. Similarly, a measure of smoking or tobacco use was considered in only 4/133 (3%). Although it is a well-known fact that these 2 risk factors represent important drivers for a patient developing ischemic heart disease, their significance in predicting post-CABG mortality risk appears likely confounded with presence of diabetes mellitus and poor renal function, which may also be sequela of obesity or diabetes.

Although these risk models may be helpful to enhance the providers' discussions with patients during the informed consent process or support provider discussions as to treatment-related risks for adverse events, the currently published CABG mortality risk models fall short of providing clinicians with useful information to optimize postoperative care consults, to ensure continuity of post-discharge care, or to enhance LT patients' survival. While it would likely not be surprising to most clinicians that these modifiable risk factors are important considerations, the manner presented in LT risks models may give the impression that LT post-CABG mortality risk is set in stone at the time of surgery, rather than an evolving risk that can be mitigated or exacerbated at any time. Using follow-up time-period-based risks (e.g., hemoglobin A1c management or continued tobacco use), therefore, future sequential modeling approaches may be needed to help better guide post-CABG follow-up care decisions and to optimize LT post-CABG survival.

One risk factor that is potentially modifiable, but not in the traditional sense, is operative urgency or priority, meaning whether a given procedure was performed in the elective *vs.* urgent or even emergent manner with an unstable patient. As clinically relevant examples, it is important to know when to intervene in patients with active angina or acute myocardial infarction. While operating in a time sensitive manner under potentially suboptimal conditions may be unavoidable, the fact that priority or status variables have been identified so frequently as ST mortality risk factors would suggest that future research funding should be prioritized to evaluate the impact of differential pre-CABG waiting periods[16].

A limited number of CABG mortality models found preoperative medications such as nitrates, anti-platelet agents, angiotensin converting enzyme inhibitor, or anti-arrhythmic medication were associated with mortality. Given risk assessment inconsistencies, some of these medications (e.g., nitrates) may have been markers for the severity of coronary disease or preoperative instability. Other medications may, in fact, be markers of optimal medical management during the pre- and postoperative periods[17].

Currently, no risk models incorporate direct measures of adherence with published clinical practice guidelines (e.g., the American College of Cardiology's guidelines for treatment of coronary artery disease) such as documenting the use of ischemic heart disease medications (e.g., pre-CABG statin use). As a potentially novel and important future enhancement to preoperative risk stratification, adherence to published guidelines should be considered. In general, adherence with published guidelines are increasingly becoming a marker used to identify high-quality, high-value care providers. Adherence to published guidelines has been shown to be suboptimal after CABG, yet adherence has been repeatedly associated with improved cardiovascular-related mortality in various populations[18-20]. Applied proactively, guideline adherence may provide a useful direction for future cardiac surgery mortality risk modeling endeavors.

Interestingly, none of these CABG mortality risk models identified mental health-related (e.g., psychiatric) or socioeconomic risk factors as predictive; however, preoperative depression has been associated with increased 5- and 10-year post-CABG mortality[21,22]. Similarly, one recent study showed a community-based marker of socioeconomic status (e.g., the Distressed Community Index) to be predictive of in-hospital mortality[23]. Hence, these types of non-traditional CABG risk factors may be worthy of future exploration.

Limitations

Conducted as an advanced PubMed literature review in February 2019, this summary has identified knowledge "gaps", which are intended to foster future CABG risk modeling research. With collaborative team member oversight and guidance, the majority of these data extractions were performed by a single author (BC). Substantial overlap was documented among several risk variables (e.g., left ventricular ejection fraction *vs.* congestive heart failure *vs.* pulmonary rales *vs.* diuretic use); therefore, the relative impact of any individual risk factor could not be easily quantified. If standardized CABG quality improvement database definitions (e.g., the Society of Thoracic Surgeons' definitions) were uniformly utilized in the future, however, comparing variable-specific relative rankings (e.g., identifying the "top five variables impacting mortality" across all published models) would become possible.

Inherently, all risk variables reported were limited to the sub-group of patients' risk characteristics uniquely captured by each database. Although a common core of risk variables was captured, each dataset may have contained unique risk factors relevant specifically to their patient populations. Additionally, different risk modeling approaches (e.g., descending stepwise logistic regression) may have contributed to the variations documented for the risk factors associated with post-CABG mortality.

In conclusion, CABG maintains an important role in the management of coronary artery disease; thus, understanding patients' ST and LT surgical risk and risk factors remains important to optimizing CABG patient's selection, treatment, and follow-up care. A wide array of CABG mortality model findings and an equally vast diversity of analytic approaches were used, each prediction model having population-specific benefits and drawbacks. Over the past 20 years, it appears that the majority of CABG registries have come to a general consensus to utilize at least a core pre-CABG risk factor set. Beyond this core dataset, however, population-relevant risk factors are commonly reported.

As always, research continues to identify new risk factors that may affect post-CABG patients' risk; based on these data-driven findings, areas warranting further research were identified - such as incorporating modifiable risk factors and ischemic heart disease guideline compliance. Additionally, a new focus appears warranted to evaluate pre-CABG wait time impacts upon surgical priority, as well as CABG risk-adjusted outcomes. Applying the lessons learned, post-CABG mortality risk model findings may be quite different in the future from current findings - as the post-CABG care continues to improve and the field of statistical risk modeling advances forward.

DECLARATIONS

Authors' contributions

Wrote the initial study protocol, under the oversight and leadership of Grover FL: Carr BM, Shroyer ALW
Prepared the research-related materials to obtain an official determination of "not research" by the Northport VA Medical Center's Research and Development office: Shroyer ALW
Performed the detailed data after implementing the advanced literature search strategy, acquisition with active involvement by Grover FL and Shroyer ALW: Carr BM
Ran the initial data analyses and prepared the initial set of tables and figures: Carr BM
Aided in the interpretation as well as the full co-author team worked collaboratively to assure a comprehensive search strategy: Grover FL, Shroyer ALW
The first draft of this article was written jointly by Carr BM and Shroyer ALW, with revisions provided by Grover FL, all co-authors provided their final approval.

Availability of data and materials

This study's data file, including data extracted for each reference listed, is available as an online-only supplement (Appendix A).

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

The Northport VA Medical Center's Research and Development Office determined that this study was "not research"; this "not research" determination was dated September 12, 2019.

Consent for publication

Not applicable.

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