



This online material has been provided to give readers additional information about this study.

eTABLE 1 Frequency of individual in-hospital complication types among participants who experienced moderate-or-severe postoperative in-hospital complications

	No Complication or Mild Complications (n = 464)	Moderate, Severe or Fatal Complications* (n= 81)
Non-fatal cardiac arrest	0 (0%)	0 (0%)
Myocardial infarction	0 (0%)	4 (5%)
Heart failure	0 (0%)	2 (2 %)
Stroke or transient ischemic attack	0 (0%)	1 (1%)
Respiratory failure	0 (0%)	7 (9%)
Pneumonia	0 (0%)	11 (14%)
Surgical site infection	0 (0%)	15 (19%)
Deep venous thrombosis	0 (0%)	1 (1%)
Pulmonary embolism	0 (0%)	2 (2%)
Dialysis	0 (0%)	2 (2%)
Major bleeding	18 (4%)	21 (26%)
Reoperation	2 (0.4%)	16 (20%)

* Individuals with moderate, severe, or fatal complications may have experienced more than one individual type of complications (e.g., surgical site infection and dialysis). Thus, the sum of individual complication types exceeds the number of individuals (n=81) who experienced moderate, severe, or fatal complications.

eTABLE 2 Frequency of individual in-hospital complication types among participants who experienced 30-day death or myocardial injury

	Alive at 30 Days Without Myocardial Injury (n=476)	30-Day Death or Myocardial Injury (n = 69)
Moderate-to-severe complications	58 (12%)	23 (33%)
Non-fatal cardiac arrest	0 (0%)	0 (0%)
Myocardial infarction	1 (0.2%)	3 (4%)
Heart failure	0 (0%)	2 (3%)
Stroke or transient ischemic attack	0 (0%)	1 (1.45%)
Respiratory failure	4 (0.8%)	3 (4%)
Pneumonia	9 (2%)	2 (3%)
Surgical site infection	12 (3%)	3 (4.35%)
Deep venous thrombosis	1 (0.2%)	0 (0%)
Pulmonary embolism	2 (0.4%)	0 (0%)
Dialysis	1 (0.2%)	1 (1%)
Major bleeding	29 (6%)	10 (14%)
Reoperation	13 (3%)	5 (7%)

* Individuals who experienced 30-day death or myocardial injury may have experienced more than one individual type of complications (e.g., surgical site infection and dialysis). Thus, the sum of individual complication types can exceed the number of individuals within each stratum.

eTABLE 3 Bivariate comparisons between patients who did versus did not suffer postoperative 30-day death or myocardial injury

Variable	Alive at 30-Days Without Myocardial Injury (N = 476)	30-Day Death or Myocardial Injury (N= 69)	P- Value
Patient characteristics			
Age (yr), mean (SD)	63 (11)	70 (9)	<0.001
Female sex, n (%)	190 (40)	25 (36)	0.56
BMI (kg m ⁻²), mean (SD)	30 (7)	29 (6)	0.29
Comorbidities, n (%)			
Coronary artery disease	79 (17)	23 (33)	<0.001
Heart failure	14 (3)	4 (6)	0.22
Cerebrovascular disease	23 (5)	8 (12)	0.023
Peripheral artery disease	14 (3)	5 (7)	0.068
Diabetes mellitus	96 (20)	16 (23)	0.56
Hypertension	294 (62)	49 (71)	0.14
Atrial fibrillation	19 (4)	6 (9)	0.081
Recent smoker*	87 (18)	7 (10)	0.095
Obstructive lung disease [†]	70 (15)	7 (10)	0.31
Arthritis	149 (31)	22 (32)	0.92
6MWT distance, mean (SD)	478 (99)	446 (100)	0.015
Renal function (n=515), n (%)‡			
eGFR ≥60 mL min ⁻¹ (1.73 m) ⁻²	406 (90)	49 (77)	0.006
eGFR 30 to 59 mL min ⁻¹ (1.73 m) ⁻²	41 (9)	13 (20)	
eGFR <30 mL min ⁻¹ (1.73 m) ⁻² or dialysis	4 (1)	2 (3)	
Natriuretic peptide concentration (n=515), n (%)			
NT pro-BNP <100 ng/L	251 (56)	19 (29)	<0.001
NT pro-BNP 100 ng/L to <300 ng/L	139 (31)	24 (38)	
NT pro-BNP ng/L ≥300 ng/L	61 (13)	21 (33)	
ASA Physical Status Score, n (%)			
1	21 (4)	1 (1)	0.15
2	274 (58)	33 (48)	
3	175 (37)	33 (48)	
4	6 (1)	2 (3)	
Revised Cardiac Risk Index (n=518), n (%)¶			
Class 1	156 (34)	11 (17)	0.002
Class 2	204 (45)	28 (43)	
Class 3	75 (17)	20 (31)	
Class 4	18 (4)	6 (9)	
Operative Characteristics			
Procedure type, n (%)			
Vascular	10 (2)	7 (10)	0.002
Intra-thoracic	22 (5)	0 (0)	

Intra-peritoneal or retro-peritoneal	157 (33)	22 (32)
Urologic or gynecologic	132 (28)	25 (36)
Head-and-neck	53 (11)	4 (6)
Orthopedic	81 (17)	7 (10)
Other	21 (4)	4 (6)

Abbreviations: 6MWT, 6-minute walk test; eGFR, estimated glomerular filtration rate; NT pro-BNP, N-terminal pro-B-type natriuretic peptide

* Current smoker or quit within previous one year

† Prior diagnosis of asthma, reactive airways disease, chronic obstructive lung disease, chronic bronchitis, or emphysema

‡ Estimated glomerular filtration rate was calculated using the preoperative serum creatinine concentration and Chronic Kidney Disease Epidemiology Collaboration equation.

¶ Revised Cardiac Risk Index scores were calculated using a modified definition of diabetes mellitus (i.e. any prior diagnosis of diabetes mellitus, as opposed to requirement for insulin therapy).

eTABLE 4 Reasons for early termination of cardiopulmonary exercise testing (CPET) among the 501 participants who attempted CPET

Reason for CPET Early Termination	Number (%)
Terminated Early	67 (13)
Fatigue	19 (28)
Shortness of breath or palpitations	6 (9)
Unable to pedal (arthritis/claudication)	23 (34)
Unable to tolerate mouthpiece	9 (13)
Safety (ATS guideline)	10 (15)

eTABLE 5 Adjusted association of the 6MWT distance with outcomes of interest in sensitivity analyses

	Odds Ratio (95% CI)	P-Value
Moderate-or-Severe Complications		
<i>Primary analysis*</i>		
Per 100 m decrease	1.32 (1.01 to 1.73)	0.045
<i>Bootstrap internal validation†</i>		
Per 100 m decrease	1.32 (1.02 to 1.75)	NA
<i>Arthritis included as an additional covariate*</i>		
Per 100 m decrease	1.32 (1.01 to 1.74)	0.044
<i>Obstructive lung disease as an additional covariate*</i>		
Per 100 m decrease	1.33 (1.02 to 1.75)	0.037
<i>Diabetes mellitus as an additional covariate*</i>		
Per 100 m decrease	1.30 (0.99 to 1.71)	0.058
30-Day Death or Myocardial Injury		
<i>Primary analysis</i>		
6MWT Distance‡	Non-linear association	0.49
<i>Age, sex and Revised Cardiac Risk Index as only covariates</i>		
6MWT Distance‡	Non-linear association	0.47

* Model c-index increased from 0.68 to 0.69 with the inclusion of either obstructive lung disease or diabetes mellitus as additional co-variables. The c-index was 0.68 when arthritis was included as an additional covariate.

† Bootstrap internal validation with 1000 samples and bias-corrected 95% confidence intervals.

‡ Modeled using a restricted cubic spline function with four knots (to account for non-linear association of 6MWT distance with the outcome)

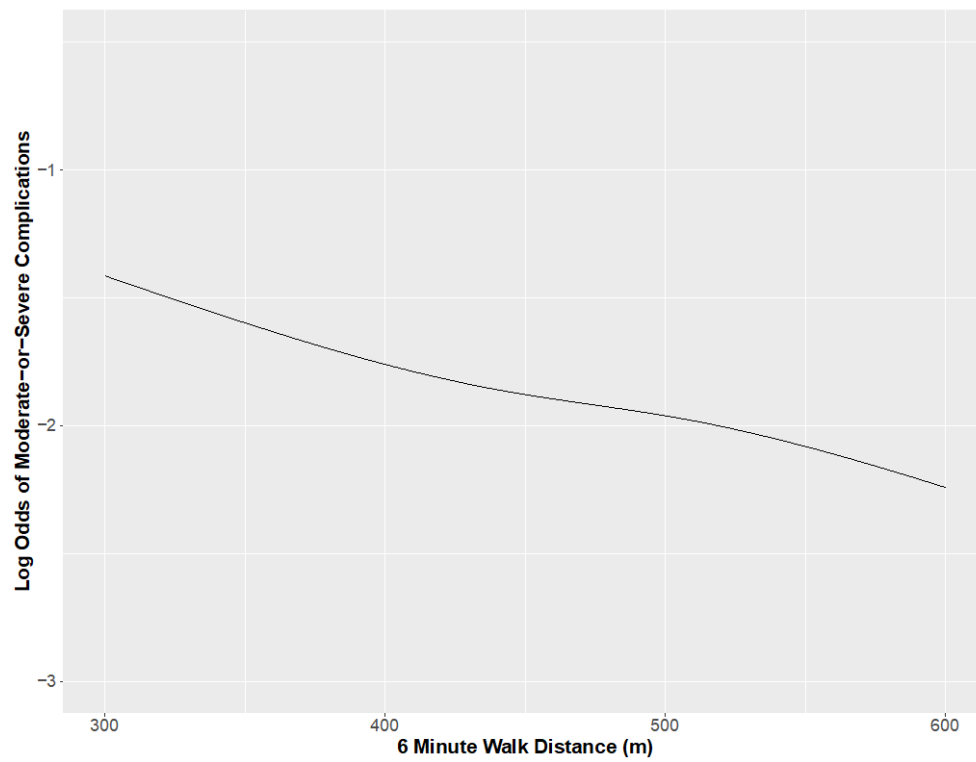
eTABLE 6 Adjusted association of 6MWT distance and other clinical risk factors with postoperative in-hospital moderate-or-severe complications

Risk factor	Beta Coefficient	Standard Error	P-value
6MWT Distance	-0.4482	0.002	0.004
Same-day CPET and 6MWT	-1.9715	1.2130	0.10
Interaction term	0.0052	0.0026	0.045
Surgical Procedure			
Moderate-risk procedure		Reference	
High-risk procedure	1.2947	0.2697	<0.001
Sex			
Male		Reference	
Female	-0.4683	0.2797	0.094
Age			
Per 1-year increase	0.0086	0.0126	0.49

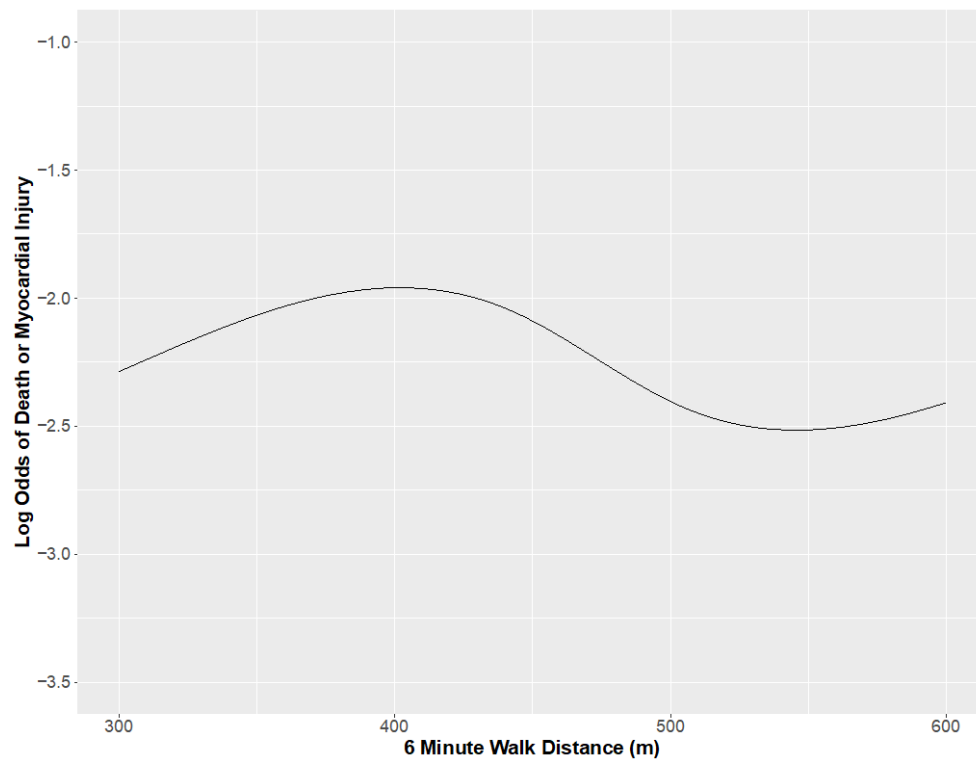
Abbreviations: CPET; cardiopulmonary exercise test; SE, standard error; 6MWT, 6-minute walk test.

Model was fit using the complete substudy cohort dataset (N=545). The multivariable regression model had a c-index of 0.71 and Hosmer-Lemeshow goodness-of-fit statistic *P*-value of 0.32. The addition of (i) 6MWT distance, (ii) presence of same-day CPET and 6MWT, and (iii) interaction of these former 2 terms to a simpler regression model with only high-risk surgery, sex and age as covariates led to an increase in the c-index from 0.67 to 0.71 (*P* = 0.059), continuous Net Reclassification Improvement of 0.29 (95% CI, 0.08 to 0.50; *P* = 0.008) and Integrated Discrimination Improvement of 0.020 (95% CI, 0.007 to 0.033; *P* = 0.002).

eFig. 1 Adjusted association of preoperative 6MWT distance (modeled using restricted cubic splines) with odds (log transformation) of moderate-or-severe in-hospital complications



eFig. 2 Adjusted association of preoperative 6MWT distance (modeled using restricted cubic splines) with odds (log transformation) of 30-day death or myocardial injury



References

1. *Wijeysundera DN, Pearse RM, Shulman MA, et al.* Assessment of functional capacity before major non-cardiac surgery: an international, prospective cohort study. *Lancet* 2018; 391: 2631-40.
2. *Dindo D, Demartines N, Clavien P-A.* Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; 240: 205-13.