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Risk Profile and Outcomes of Patients Requiring Coronary Revascularization as Concomitant Procedure to Repair of Type A Aortic Dissection



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ABSTRACT

BACKGROUND The present study aimed to report the early and late clinical outcomes of patients who underwent surgical repair for acute type A aortic dissection requiring concomitant coronary artery bypass grafting (CABG), and to explore potential risk factors associated with the need for this additional procedure.

METHODS Data were retrieved from the multicenter European Registry of Type A Aortic Dissection (ERTAAD). Bootstrapped least absolute shrinkage and selection operator logistic regression and multilevel multivariate logistic regression were performed for variable selection to identify predictors of hospital death, and logistic regression was used for the prediction of CABG.

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RESULTS A total of 292 (8.04%) of 3633 patients required additional CABG. The in-hospital mortality rate was 33% for patients undergoing CABG vs 16% of non-CABG recipients ($P < .001$; odds ratio [OR], 2.52; 95% CI, 1.93–3.35). Dissection of the aortic root involving the right coronary cusp ($P < .001$; OR, 7.83; 95% CI, 5.55–11.0), a tear in the aortic root ($P = .002$; OR, 2.08; 95% CI, 1.29–3.32), mitral valve insufficiency ($P = .034$; OR, 1.33; 95% CI, 1.01–1.71), and a genetic syndrome ($P < .001$; OR, 3.23; 95% CI, 1.66–5.99) independently predicted the need for CABG.

CONCLUSIONS The need for additional CABG is not a rare occurrence during repair of type A aortic dissection and is associated with an increased mortality risk. Intimal tear localization and right coronary sinus dissection should be carefully examined in the preoperative image evaluation to stratify the risk of revascularization and plan the most appropriate approach.

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Surgical repair of acute type A aortic dissection (TAAD) is still associated with significant mortality rates. In this regard, large registries report mortality rates of approximately 18%.^{1–3} Moreover, the mortality rate increases in the presence of myocardial ischemia. This can occur if dissection of coronary ostia determines cardiac malperfusion. Other possible causes of ischemia during TAAD repair include unknown coronary artery disease, inadequate myocardial protection secondary to improper delivery of cardioplegia in dissected coronary arteries, prolonged aortic cross-clamp time, and complications related to coronary button reimplantation during aortic root replacement. In this setting, prompt intervention, such as additional coronary artery bypass grafting (CABG), can reduce cardiac ischemia and help prevent heart failure.

To date, only a few single-center studies have been reported on this topic in the current literature,^{4,5} and their limited number of observations jeopardizes a deep analysis of patient outcomes requiring concomitant CABG. This study, which was based on a large multicenter data set, provides a comprehensive overview of postoperative outcomes in these patients. Moreover, it explores the central hypothesis that CABG can be predicted preoperatively, which could help refine surgical strategies and improve patient outcomes.

PATIENTS AND METHODS

STUDY POPULATION AND END POINTS. The present analysis is based on the data of 3633 consecutive patients from the European Registry of Type A Aortic Dissection (ERTAAD). This registry comprises data from a multicenter, retrospective

cohort including consecutive patients operated on for acute TAAD at 17 centers of cardiac surgery located in 8 European countries (Belgium, Czech Republic, Finland, France, Germany, Italy, Spain, and the United Kingdom) from January 2005 to March 2021. Patients with iatrogenic aortic dissection were excluded from the study. On the basis of the foregoing hypotheses, the primary end point was the outcome analysis, which included in-hospital complications and in-hospital and late mortality. The second end point was the development of a prediction model for CABG on the basis of preoperative variables.

The Institutional Review Board and Ethics Committee of the University Hospital Muenster (June 18, 2021, diary No. 2021-368-f-S) approved this retrospective study. According to the approval, individual informed consent was not required in this retrospective analysis and was therefore waived. The ERTAAD was registered in [ClinicalTrials.gov](https://clinicaltrials.gov) with the identifier [NCT04831073](https://clinicaltrials.gov/ct2/show/study?term=NCT04831073).

DATA PREPROCESSING AND ANALYSIS. Continuous variables are presented as median and interquartile differences. Categorical variables are shown as counts and percentages. Differences between patients undergoing and not undergoing CABG were obtained using the Wilcoxon rank sum test for continuous variables and the Pearson χ^2 test or the Fisher exact test for categorical variables. Imputation methods for missing variables are reported in the [Supplemental Methods](#), [Supplemental Figure 1](#), and [Supplemental Tables 1 and 2](#).

A bootstrapped least absolute shrinkage and selection operator (LASSO) logistic regression was performed for variable (feature) selection to identify key predictors of hospital death and remove nonpredictive variables. The final step of our

TABLE 1 Baseline Characteristics of the Study Cohorts

Characteristic	Overall, N = 3633	Non-CABG, n = 3341	CABG, n = 292	p Value
Demographics				
Estimated distance to hospital, km	28 (8–60)	29 (9–60)	22 (6–60)	.11
Age, y	64 (54–74)	64 (54–74)	64 (54–73)	.5
Octogenarians	296 (8.1)	275 (8.2)	21 (7.2)	.5
Female	1093 (30)	1010 (30)	83 (28)	.5
Laboratory values				
eGFR CKD–EPI, mL/min/1.73 m ²	69 (52–87)	69 (52–87)	70 (54–87)	.8
Arterial lactate, mmol/L	1.60 (1.00–2.80)	1.60 (1.00–2.79)	1.80 (1.10–3.25)	.075
Comorbidities				
Genetic syndromes	78 (2.1)	59 (1.8)	19 (6.5)	<.001
Marfan syndrome	71 (2.0)	53 (1.6)	18 (6.2)	<.001
Loeys–Dietz syndrome	5 (0.1)	5 (0.1)	0 (0)	>.9
Ehlers–Danlos syndrome	2 (<0.1)	1 (<0.1)	1 (0.3)	.2
Aortitis	14 (0.4)	14 (0.4)	0 (0)	.6
Family history of aortic dissection	114 (3.1)	104 (3.1)	10 (3.4)	.8
Previous cardiac surgery	80 (2.2)	70 (2.1)	10 (3.4)	.14
Hypertension	2582 (71)	2379 (71)	203 (70)	.5
Diabetes	171 (4.7)	157 (4.7)	14 (4.8)	>.9
Previous stroke	139 (3.8)	130 (3.9)	9 (3.1)	.5
Previous transient ischemic attack	78 (2.1)	73 (2.2)	5 (1.7)	.6
Pulmonary disease	305 (8.4)	283 (8.5)	22 (7.5)	.6
Extracardiac arteriopathy	180 (5.0)	161 (4.8)	19 (6.5)	.2
Medications				
Aspirin	672 (18)	602 (18)	70 (24)	.012
Antiplatelet drugs	190 (5.2)	166 (5.0)	24 (8.2)	.017
Clopidogrel	144 (4.0)	126 (3.8)	18 (6.2)	.044
Ticagrelor	36 (1.0)	30 (0.9)	6 (2.1)	.064
Ticlopidine	7 (0.2)	7 (0.2)	0 (0)	>.9
Direct oral anticoagulant	82 (2.3)	73 (2.2)	9 (3.1)	.3
Preoperative findings				
Preoperative cardiac massage	163 (4.5)	140 (4.2)	23 (7.9)	.004
Cardiogenic shock requiring inotropes	626 (17)	566 (17)	60 (21)	.12
Unconsciousness before sedation	148 (4.1)	135 (4.0)	13 (4.5)	.7
Hemiplegia or hemiparesis	292 (8.0)	269 (8.1)	23 (7.9)	>.9
Paraplegia or paraparesis	73 (2.0)	67 (2.0)	6 (2.1)	>.9
Cerebral malperfusion	807 (22)	738 (22)	69 (24)	.5
Spinal malperfusion	73 (2.0)	67 (2.0)	6 (2.1)	>.9
Renal malperfusion	356 (9.8)	333 (10.0)	23 (7.9)	.2
Mesenteric malperfusion	157 (4.3)	148 (4.4)	9 (3.1)	.3
Peripheral malperfusion	536 (15)	496 (15)	40 (14)	.6
Penn classification				.078
A	2035 (56)	1883 (56)	152 (52)	

TABLE 2 Operative Data

Variable	Overall, N = 3633	Non-CABG, N = 3341	CABG, N = 292	p Value
Intraoperative findings				
Dissection of aortic root involving noncoronary cusp	727 (20)	655 (20)	72 (25)	.039
Dissection of aortic root involving right coronary cusp	622 (17)	487 (15)	135 (46)	<.001
Dissection of aortic root involving left coronary cusp	351 (9.7)	298 (8.9)	53 (18)	<.001
Dissection of the aortic arch	3066 (85)	2835 (85)	241 (83)	.4
Dissection of the descending thoracic aorta	1942 (53)	1774 (53)	168 (58)	.14
Tear in aortic root	594 (16)	501 (15)	93 (32)	<.001
Tear in ascending aorta	2378 (65)	2207 (66)	171 (59)	.010
Tear in aortic arch	613 (17)	575 (17)	38 (13)	.066
Aortic valve insufficiency				<.001
1	763 (21)	708 (21)	55 (19)	
2	579 (16)	533 (16)	46 (16)	
3	693 (19)	601 (18)	92 (32)	
Mitral valve insufficiency				.010
1	440 (15)	395 (15)	45 (19)	
2	46 (1.6)	37 (1.4)	9 (3.7)	
3	17 (0.6)	15 (0.6)	2 (0.8)	
SURGICAL PROCEDURE				
Right subclavian axillary artery cannulation	1495 (41)	1366 (41)	129 (44)	.3
Femoral artery cannulation	1152 (32)	1062 (32)	90 (31)	.7
Supracoronary replacement	2569 (71)	2443 (73)	126 (43)	<.001
Aortic root replacement	1064 (29)	898 (27)	166 (57)	<.001
Bentall procedure	850 (23)	700 (21)	150 (51)	<.001
David procedure	146 (4.0)	135 (4.0)	11 (3.8)	.8
Yacoub procedure	68 (1.9)	63 (1.9)	5 (1.7)	.8
Partial root repair	286 (7.9)	267 (8.0)	19 (6.5)	.4
Aortic valve replacement	193 (5.3)	181 (5.4)	12 (4.1)	.3
Mitral valve repair	14 (0.4)	11 (0.3)	3 (1.0)	.10
Mitral valve replacement	4 (0.1)	4 (0.1)	0 (0)	>.0.9
Tricuspid valve repair	5 (0.1)	5 (0.1)	0 (0)	>.9
Anastomosis to the distal ascending aorta	918 (25)	837 (25)	81 (28)	.3
Beveled hemiarch repair	1624 (45)	1491 (45)	133 (46)	.8
Total aortic arch repair	543 (15)	499 (15)	44 (15)	>.9
Frozen elephant trunk	215 (5.9)	195 (5.8)	20 (6.8)	.5
TEVAR completion	26 (0.7)	25 (0.7)	1 (0.3)	.7
TEVAR during index hospitalization	8 (0.2)	7 (0.2)	1 (0.3)	.5
Myocardial ischemic time, min	110 (80–152)	107 (79–147)	157 (111–195)	0.001
Cardiopulmonary bypass time, min	204 (162–260)	199 (160–252)	272 (220–346)	<.001

Values are n (%), median (interquartile range), or P. CABG, coronary artery bypass grafting; TEVAR, thoracic endovascular aortic repair.

analysis consisted of a multilevel multivariate logistic regression, which is advantageous for clustered data, such as

patients (35.5%) continued to show signs of heart failure. A total of 232 patients (79.5%) received 1 single graft, 41 patients (14%) had 2 distal anastomoses, 16 patients (5.5%) had 3, and 3 patients (1%) had 4. A complete analysis of the data set indicated that nearly one-half (46.7%) of the bypasses were directed to the right coronary artery (RCA), followed by approximately one-third to the left anterior descending artery (31.11%), whereas lateral wall vessels accounted for 22.22% of the grafts.

Patients undergoing CABG were more likely to have a genetic syndrome (6.5% vs 1.8%; $P < .001$). Moreover, they were preoperatively in significantly worse hemodynamic condition, as testified by the higher rates of preoperative cardiac massage (7.9% vs 4.2%; $P < .001$). (Baseline characteristics of both groups are presented in [Table 1](#).⁶)

In patients who underwent CABG, localization of the intimal tear was significantly more frequent in the aortic root (32% vs 15%; $P < .001$) with a significantly higher proportion of dissection of the right and left coronary sinuses (46% vs 15% and 18% vs 8.9%; both $P < .001$) than the noncoronary sinus ($P = .039$). Moreover, these patients had higher rates of mitral and aortic valve insufficiency ($P < .001$ and $P = .010$, respectively).

The rate of aortic root replacement in CABG recipients was more than twice that in the remaining patients who did not undergo CABG (57% vs 27%; $P < .001$). (Intraoperative differences between both groups are displayed in [Table 2](#).) Of these 166 patients who underwent root replacement and concomitant CABG, 108 had coronary dissection caused by root dissection involving either the right or left coronary sinus. In 32 patients, there was root dissection without overt coronary involvement. In the remaining 26 patients, neither root dissection nor coronary artery dissection was identified.

CLINICAL RESULTS AND PREDICTION OF CABG. Patients who underwent concomitant revascularization had a significantly higher probability of undergoing venoarterial extracorporeal membrane oxygenation (13% vs 1.9%; $P < .001$), renal replacement therapy (18% vs 10%; $P < .001$), and tracheostomy (14% vs 7.9%; $P = .001$). Postoperative outcomes are shown in [Table 3](#).

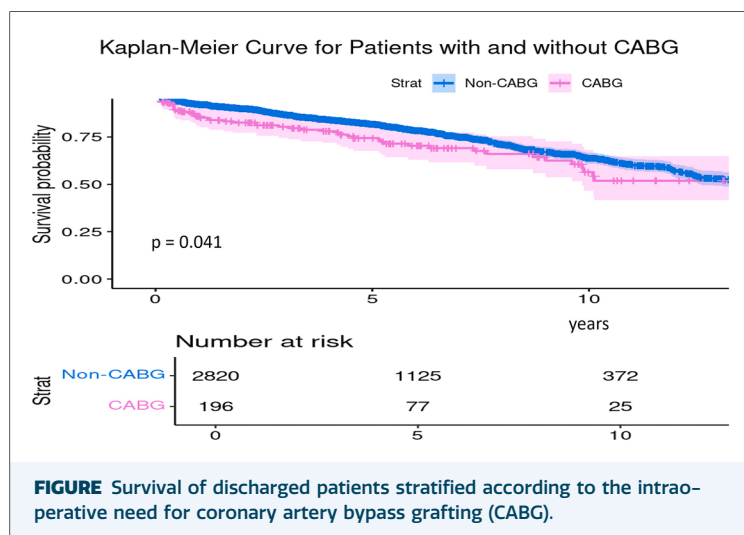
The overall mortality rate was 17% ($n = 617$), with an intraclass correlation coefficient of .0715, indicating that 7.15% of the variance in mortality was attributable to between-hospital differences. Stratifying mortality rates, patients undergoing additional CABG showed 2.52 times the odds of in-hospital

TABLE 3 Postoperative Outcomes

Variable	Overall, N = 3633	Non-CABG, n = 3341	CABG, n = 292	P Value
Hospital death	617 (17)	521 (16)	96 (33)	<.001
Ischemic stroke	492 (14)	442 (13)	50 (17)	.062
Hemorrhagic stroke	67 (1.8)	62 (1.9)	5 (1.7)	.9
Global brain ischemia	168 (4.6)	148 (4.4)	20 (6.8)	.059
Paraparesis or paraplegia	188 (5.2)	165 (4.9)	23 (7.9)	.030
Mesenteric ischemia	139 (3.8)	129 (3.9)	10 (3.4)	.7
Temporary dialysis	398 (11)	345 (10)	53 (18)	<.001
Permanent dialysis	141 (3.9)	122 (3.7)	19 (6.5)	.015
Laryngeal nerve palsy	71 (2.0)	65 (1.9)	6 (2.1)	.9
Reoperation or intrathoracic bleeding	515 (14)	464 (14)	51 (17)	.093
Tracheostomy	301 (8.3)	261 (7.8)	40 (14)	<.001
Deep sternal wound infection or mediastinitis	84 (2.3)	81 (2.4)	3 (1.0)	.13
Intraoperative heart failure	498 (14)	395 (12)	103 (35)	<.001
VA-ECMO	100 (2.8)	62 (1.9)	38 (13)	<.001
ICU stay, d	5 (3–11)	5 (3–11)	6 (2–14)	.4

Values are n (%), median (interquartile range), or P. CABG, coronary artery bypass grafting; ICU, intensive care unit; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

death compared with patients who did not undergo CABG. The mortality rate of CABG recipients was 33% ($n = 96$) vs 16% of patients who did not undergo CABG ($n = 521$) (adjusted $P < .001$). ([Table 4](#) presents all significant risk factors for in-hospital mortality, whereas the odds ratios [ORs] from the LASSO analysis are reported in [Supplemental Table 3](#).) On December 31



CI, 1.08-1.87). (The results of Cox regression model are reported in [Supplemental Table 4](#), [Supplemental Figure 2](#), and the [Supplemental Methods](#).) The [Figure](#) shows the Kaplan-Meier curves with the log-rank test ($P = .041$).

At the multivariate regression analysis, genetic syndromes ($P < .001$; OR, 3.23), mitral valve insufficiency ($P = .034$; OR, 1.33), a tear in the aortic root ($P = .001$; OR, 2.08), and dissection of the aortic root involving the right coronary cusp ($P < .001$; OR, 7.83) were independent predictors of the need for additional CABG ([Table 5](#)) (C-statistic = 0.74). In a further subanalysis including intraoperative variables, aortic root replacement did not predict the need for concomitant CABG ($P = .11$). The rate of CABG in patients without risk factors was 4.2%, increasing to 20.3% in patients with 1 or more risk factors.

COMMENT

The main aims of the study of this multicenter registry were to report and validate the clinical

results of the few single-center studies reporting the concomitant CABG during repair for acute TAAD. Additionally, because of the high number of patients, we further aimed to develop a prediction model for the need for CABG on the basis of preoperative variables. The first results of the current study are that additional CABG is not a rare occurrence, accounting for a rate of 8.04%, and it is associated with 2.52 times the odds of in-hospital death compared with patients who do not undergo CABG during the repair of TAAD. Moreover, some of the preoperative imaging data, such as dissection of the aortic root involving the right coronary cusp, a tear in the aortic root, and other clinical variables such as the presence of mitral valve insufficiency genetic syndrome can independently predict the need for CABG.

Tong and colleagues,⁷ in a study of 1018 patients, reported a CABG rate of 7.3%. In a recent publication by Morjan and colleagues,⁸ the rate of the concomitant CABG procedure was 10.7%. Including patients aged more than 70 years from the GERAADA registry ($n = 1558$), Rylski and colleagues⁹ reported an incidence of 16.6%. In the latter study, a considerable difference in CABG rate was found between patients aged more than 80 years (9.4%) and aged between 70 and 80 years (18.1%). The higher probability of undergoing CABG in younger patients can be explained by the finding that younger patients had a higher risk profile than older patients, for whom a stricter selection for surgical referral was made.

In the present study, a total of 158 patients (54.1%) underwent CABG because of injury of the coronary ostia. This finding aligns closely with those of another single-center study by Morjan and colleagues,⁸ in which 68.3% of the CABG indications were the result of coronary dissection. In that study, the RCA was also the most commonly grafted vessel (63.4%), followed by the left anterior descending artery (26.8%).

In our multivariate analysis, patients with dissection of the aortic root involving the right coronary cusp yielded the highest odds in the prediction model for CABG, a finding supporting the fact that the RCA was the most frequently grafted vessel. Another interesting finding was that patients with a genetic syndrome had a significantly higher rate of undergoing CABG. In this regard, coronary wall fragility may predispose patients to a higher probability of complex coronary dissection requiring demanding repair and thus justifying the need for CABG.

TABLE 5 Multivariate Model for the Prediction of the Need for Additional Coronary Artery Bypass Grafting

Characteristic	OR	95% CI	p Value
Genetic syndromes	3.23	1.66-5.99	<.001
Mitral valve insufficiency	1.33	1.01-1.71	.034
Tear in the aortic root	2.08	1.29-3.32	.002
Dissection of aortic root involving noncoronary cusp	0.51	0.35-0.74	<.001
Dissection of aortic root involving right coronary cusp	7.83	5.55-11.0	<.001

OR, odds ratio.

Another unexpected risk factor was preoperative mitral insufficiency. In this regard, a possible cause is myocardial ischemia secondary to coronary malperfusion, leading to papillary muscle dysfunction. Another possible explanation is that CABG recipients have a higher incidence of aortic valve insufficiency ($P < .001$), given the significantly higher proportion of aortic root dissections, that may have ultimately contributed to left ventricular dilatation, thereby worsening the degree of mitral regurgitation.

As a consequence of this analysis, an attentive evaluation of the patient's history and the available imaging should focus on the aortic root for possible coronary ostial dissection and on the coronary course for possible native coronary disease, representing an important step for surgeons to stratify the risk of ischemia.

A recent study by Pitts and colleagues⁵ that included patients with preoperative cardiac malperfusion found a significant increase in 30-day mortality among patients who underwent bailout CABG (81%) as compared with patients with planned CABG (mortality rate, 48%). In case of injury of the coronary ostia, myocardial protection through appropriate cardioplegia delivery and complex repair of the coronary ostia can undermine the success of the operation. These evaluations can help consider planning CABG first and not as a rescue procedure. Performing CABG first can mitigate intraoperative ischemia by delivering cardioplegia through the graft.

In line with this strategy, Kreibich and colleagues,¹⁰ in a study of 76 patients with coronary malperfusion, recommended a CABG procedure in all patients in whom the cardioplegic solution could not be delivered adequately, as well as in patients with coronary avulsion. In that study, the mortality rate of this subset of patients was slightly higher (24%) than the overall mortality in many multicenter reports,^{1–3} thus speculating that this management approach may reduce mortality and possibly lower the risk of intraoperative ischemia.

Our study has some inherent limitations. First, the retrospective design of this registry is a main source of potential biases. Given the emergency nature of treatment for aortic dissection, the lack of preoperative angiography limits the ability to provide a detailed assessment of the coronary

anatomy and of the possible presence of lesions that could have caused intraoperative ischemia and be a potential indication for additional CABG. Moreover, the combined effects of coronary malperfusion, improper delivery of cardioplegia, and prolonged clamping time cannot be fully disentangled. It also cannot be ruled out that coronary malperfusion may occur immediately after aortic root repair in response to a progression of dissection in the reconstructed root. For these reasons, we urge caution when attempting to define the indications for CABG in emergency settings precisely. Furthermore, the Neri classification,¹¹ which provides information about the type of coronary lesion, was not reported.

Although data on deaths of all patients were collected retrospectively from electronic national registries as well as by contacting regional hospitals, patients, and their relatives and from planned control visits, we estimated that 17.1% of patients did not have follow-up data on December 31, 2020. In fact, because of the acute nature of TAAD, many patients were not residents of the hospital catchment areas.

Despite these limitations, this study provides a comprehensive overview of the incidence, mortality, and risk profile of patients undergoing repair of TAAD and needing CABG. In conclusion, the need for additional CABG is not infrequent during the repair of TAAD and is associated with an increased mortality risk. Coronary anatomy, localization of intimal tear, and dissection of a coronary sinus should be carefully examined in the preoperative image evaluation to stratify the risk of revascularization and plan the best appropriate approach.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the authors used Grammarly in order to review spelling and grammar. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Atherosclerosis or Dissection: Cause, Consequence, or Coincidence?



INVITED COMMENTARY:

In this issue of *The Annals of Thoracic Surgery*, Dell'Aquila and colleagues¹ report the results of acute type A aortic dissections (ATAAD) with concomitant coronary artery bypass grafting (CABG), drawing from the comprehensive European Registry of Type A Dissection (ERTRAAD). This large multicenter study sheds light on an infrequently examined subset of patients with ATAAD, reporting a concomitant CABG rate of 8%. The incidence of concomitant CABG at the time of ATAAD repair has been reported as high as 16% in the German Registry for Acute Aortic Dissection Type A (GERAADA) registry² and as low as 4% in the International Registry of Acute Aortic Dissection (IRAD) cohort.³

One of the key points in this study is the increased in-hospital mortality with concomitant CABG compared with no CABG (33% vs 16%). Although this trend has been seen in smaller studies, the authors go further to investigate predictors and risk factors for concomitant CABG, which include right coronary cusp involvement,</