Table 1 of the supplementary data. Number of included patients, inclusion period, and responsible investigators by participating center

Participating centers/Responsible investigators	Inclusion period of	Number of patients included
Quebec Heart & Lung Institute (Canada) Dr Josep Rodes-Cabau	2014-2023	2084
Hôpital Cardiologique Haut-Lévêque (France) Dr Julien Ternacle	2016-2020	1105
Bichat–Claude Bernard Hospital (France) Dr Marina Urena	2015-2020	724
Hospital Central de Asturias (Spain) Dr Alberto Alperi	2015-2020	668
Southlake Regional Health Centre Newmarket (Canada) Dr Asim Cheema	2016-2020	656
Hospital Marqués de Valdecilla (Spain) Dr Gabriela Veiga-Fernandez	2015-2021	651
Hospital Clínico San Carlos (Spain) Dr Luis Nombela-Franco	2015-2020	520
Hospital Germans Trias i Pujol (Spain) Dr Victoria Vilalta	2016-2021	494
Naples Federico II (Italy) Dr Giovanni Esposito	2015-2022	460
Toulouse University Hospital (France) Dr Francisco Campelo-Parada	2014-2019	453
Magna Graecia' University (Italy) Dr Ciro Idolfi	2015-2021	413
Hospital Puerta Hierro (Spain) Dr Maria del Trigo	2016-2022	390
Hospital Regional Virgen de la Victoria (Spain) Dr Antonio Munoz-Garcia	2017-2020	348
Hospital Doce de Octubre (Spain) Dr Nicolas Maneiro	2016-2022	338
Hospital de la Santa Creu i Sant Pau (Spain) Dr Luis Asmarats	2018-2020	245

Hospital Clínic de Barcelona (Spain) Dr Ander Regueiro	2016-2019	219
Hospital La Princesa (Spain) Dr David del Val	2016-2020	196
Hospital Vall d´Hebron (Spain) Dr Vicenç Serra	2016	67
Rennes University Hospital (Spain) Dr Vincent Auffret	2018	47

Table 2 of the supplementary data. Individual early safety endpoint definitions according to VARC-3 criteria

VARC-3 individual endpoint	VARC-3 definition	**Study definition** (Identical, modified, not available)
All-cause mortality	Defined as 30-day or in-hospital cardiovascular or noncardiovascular mortality.	Identical
Stroke	Ischemic, hemorrhagic or not otherwise specified were included.	Identical
Bleeding type 2, 3, and 4	• Type 2: *a)* overt bleeding requiring a transfusion of 2-4 units of whole blood/red blood cells; *b)* overt bleeding associated with a hemoglobin drop of > 3 g/dL (> 1.86 mmol/L) but < 5 g/d (< 3.1 mmol/L). • Type 3: *a)* overt bleeding in a critical organ, such as intracranial, intraspinal, intraocular, pericardial (associated with hemodynamic compromise/tamponade and necessitating intervention), or intramuscular with compartment syndrome; *b)* overt bleeding causing hypovolemic shock or severe hypotension (systolic blood pressure < 90 mmHg lasting > 30 min and not responding to volume resuscitation) or requiring vasopressors or surgery*; d)* overt bleeding requiring reoperation, surgical exploration, or reintervention for the purpose of controlling bleeding; *e)* postthoracotomy chest tube output ≥ 2L within a 24-h period; *f)* overt bleeding requiring a transfusion of ≥ 5 units of whole blood/red blood cells; *g)* overt bleeding associated with a hemoglobin drop ≥ 5 g/dL (≥ 3.1 mmol/L). • Type 4: overt bleeding leading to death. Should be classified as: probable: clinical suspicion or definite: confirmed by autopsy or imaging.	Identical
Major vascular complication	One of the following: *a)* Aortic dissection or aortic rupture. *b)* Vascular (arterial or venous) injury (perforation, rupture, dissection, stenosis, ischemia, arterial or venous thrombosis including pulmonary embolism, arteriovenous fistula, pseudoaneurysm, hematoma, retroperitoneal hematoma, infection) or compartment syndrome resulting in death, VARC type ≥ 2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment. *c)* Distal embolization (noncerebral) from a vascular source resulting in death, amputation, limb or visceral ischemia, or irreversible end-organ damage. *e)* Unplanned endovascular or surgical intervention resulting in death, VARC type ≥ 2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment. f) Closure device failure resulting in death, VARC type ≥ 2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment.	Identical
Major access-related complication	One of the following: a) Nonvascular structure, noncardiac structure perforation, injury, or infection resulting in death, VARC type ≥ 2 bleeding, irreversible nerve injury or requiring unplanned surgery or percutaneous intervention. b) Nonvascular access site (eg, transapical left ventricular) perforation, injury, or infection resulting in death, VARC type ≥ 2 bleeding, irreversible nerve injury or requiring unplanned surgery or percutaneous intervention.	Identical
Major cardiac structural complications	One of the following:	Identical

	a) Cardiac structure perforation, injury, or compromise resulting in death, VARC type ≥2 bleeding, hemodynamic compromise or tamponade, or requiring unplanned surgical or percutaneous intervention. *b)* New pericardial effusion resulting in death, VARC type ≥ 2 bleeding, hemodynamic compromise or tamponade, or requiring unplanned surgical or percutaneous intervention. *c)* Coronary obstruction resulting in death, hemodynamic compromise, myocardial infarction, or unplanned surgical or percutaneous intervention. Coronary obstruction may be acute (during the procedure) or delayed (after completion of the procedure). *d)* Coronary artery access difficulties for needed coronary angiography or intervention, resulting in death, hemodynamic compromise, myocardial infarction, coronary or aortic root injury, compromise in aortic valve prosthesis integrity, unplanned surgical or percutaneous intervention, or the inability to perform the intended procedure.	
Acute kidney injury type 3, and 4	• Stage 3: acute kidney disease that fulfils at least 1 of the following criteria: *a)* an increase in serum creatinine >300% (> 3.0 x increase) within 7 days compared with baseline; *b)* serum creatinine ≥ 4.0 mg/dL (≥ 354 mmol/L) with an acute increase of ≥ 0.5 mg/dL (≥ 44 micromol/L). • Stage 4: acute kidney disease requiring new temporary or permanent renal replacement therapy.	Identical
Moderate or severe aortic regurgitation	Aortic regurgitation greater than mild in the postprocedural transthoracic echocardiogram.	Identical
New permanent pacemaker	New implant due to procedure-related conduction abnormalities.	Identical
Surgical conversion or intervention	Need for a new interventional procedure or surgery.	Identical

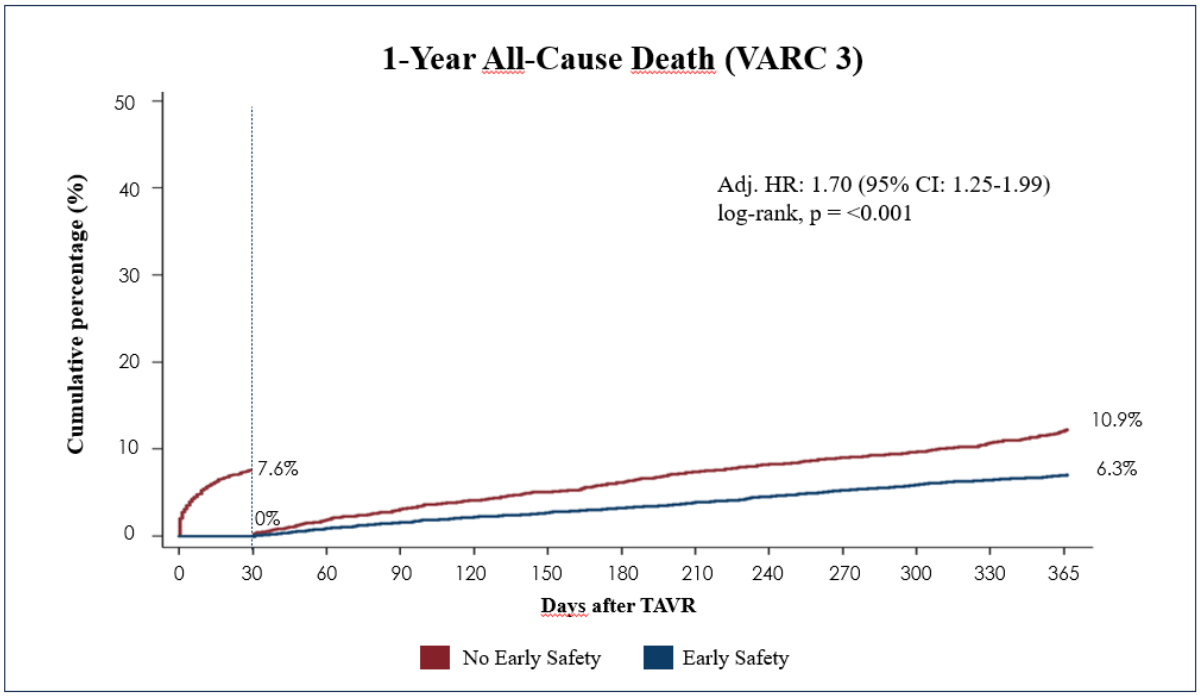
Table 3 of the supplementary data. Incidence of early safety and each individual endpoint according to VARC-3 criteria, including only type 3-4 bleeding

	Total
	N =10 078
Early safety	7433 (73.8)
All-cause death	262 (2.6)
Stroke	207 (2.1)
Bleeding type 3 and 4	426 (4.2)
Major vascular, access-related, or cardiac structural complications	800 (7.9)
Acute kidney injury type 3, and 4	296 (2.9)
Moderate or severe aortic regurgitation	46 (0.5)
New permanent pacemaker	1373 (13.6)
Surgical conversion or intervention	66 (0.7)

Table 4 of the supplementary data. Incidence of early safety and each individual endpoint according to VARC-2 criteria

	Total
	N = 10 078
Early safety	8296 (82.3)
All-cause mortality	262 (2.6)
All stroke (disabling and nondisabling)	207 (2.1)
Life-threatening bleeding	465 (4.6)
Acute kidney injury—stage 2 or 3	296 (2.9)
Coronary artery obstruction	52 (0.5)
Major vascular complication	708 (7.0)
Valve-related dysfunction requiring repeat procedure	127 (1.3)

Figure 1 of the supplementary data. Landmark analysis at 30 days with Kaplan-Meier estimates for all-cause mortality according to the presence of early safety defined as per VARC-3 criteria



Thirty-day all-cause mortality: 0% in early safety (ES) patients and 7.62% in no-ES patients (95%CI: 6.83-8.65). From 30-days to 1 year all-cause mortality: 6.30% in ES patients (95%CI: 5.72-7.01) and 10.90% in no-ES patients (95%CI: 9.83 to 12.03).