Identification of optimal device combinations for the chimney endovascular aneurysm repair technique within the PERICLES registry

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ABSTRACT

Objective: The ideal stent combination for chimney endovascular aneurysm repair remains undetermined. Therefore, we sought to identify optimal aortic and chimney stent combinations that are associated with the best outcomes by analyzing the worldwide collected experience in the PERformance of chImney technique for the treatment of Complex aortic pathoLogiES (PERICLES) registry.

Methods: The PERICLES registry was reviewed for patients with pararenal aortic disease electively treated from 2008 to 2014. Eleven different aortic devices were identified with three distinct subgroups: group A (n = 224), nitinol/polyester; group B (n = 105), stainless steel/polyester; and group C (n = 69), nitinol/expanded polytetrafluoroethylene. The various chimney stent subtypes included the balloon-expandable covered stent (BECS), self-expanding covered stent, and bare-metal stent. Deidentified aortic and chimney device combinations were compared for risk of chimney occlusion, type Ia endoleak, and survival. Effects of high-volume centers (>100 cases), use of an internal lining chimney stent, number of chimney stents, and number of chimney stent subtypes deployed were also considered. We considered demographics, comorbidities, and aortic anatomic features as potential confounders in all models.

Results: The 1- and 3-year freedom from BECS chimney occlusion was not different between groups (group A, 96% ± 2% and 87% ± 5%; groups B and C, 93% ± 3% and 76% ± 10%; Cox model, $P = .33$). Similarly, when non-BECS chimney stents were used, no difference in occlusion risk was noted for the three aortic device groupings; however, group C patients receiving BECS did have a trend toward higher occlusion risk relative to group C patients not receiving a BECS chimney stent (hazard ratio [HR], 4.0; 95% confidence interval [CI], 0.85-18.84; $P = .08$). Patients receiving multiple chimney stents, irrespective of stent subtype, had a 1.8-fold increased risk of occlusion for each additional stent (HR, 1.8; 95% CI, 1.2-2.9; $P = .01$). Use of a bare-metal endolining stent doubled the occlusion hazard (HR, 2.1; 95% CI, 1.0-4.5; $P = .05$). Risk of type Ia endoleak (intraoperatively and postoperatively) did not significantly differ for the aortic devices with BECS use; however, group C patients had higher risk relative to groups A/B without BECS (C vs B: odds ratio [OR], 3.2 [95% CI, 1-11; $P = .05$]; C vs A/B: OR, 2.4 [95% CI, 0.9-6.4; $P = .08$]). Patients treated at high-volume centers had significantly lower odds for development of type Ia endoleak (OR, 0.2; 95% CI, 0.1-0.7; $P = .01$) irrespective of aortic or chimney device combination. Mortality risk was significantly higher in group C + BECS vs group A + BECS (HR, 5.3; 95% CI, 1.6-17.5; $P = .006$). The 1- and 3-year survival for groups A, B, and C (+BECS) was as follows: group A, 97% ± 1% and 92% ± 3%; group B, 93% ± 3% and 83% ± 7%; and group C, 84% ± 7% and 63% ± 14%. Use of more than one chimney subtype was associated with increased mortality (HR, 3.2; 95% CI, 1.4-7.5; $P = .006$).

Conclusions: Within the PERICLES registry, use of nitinol/polyester stent graft devices with BECS during chimney endovascular aneurysm repair is associated with improved survival compared with other aortic endografts. However, this advantage was not observed for non-BECS repairs. Repairs incorporating multiple chimney subtypes were also associated with increased mortality risk. Importantly, increasing chimney stent number and bare-metal endolining stents increase chimney occlusion risk, whereas patients treated at low-volume centers have higher risk of type Ia endoleak. (J Vasc Surg 2018;■:1-12.)

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The use of parallel stents was first described as a "bailout" maneuver after inadvertent renal artery coverage during endovascular aneurysm repair (EVAR).[1,2] Since the initial description, there has been rapid proliferation and adoption of "chimney" techniques in the management of paravisceral aortic disease.[1,3-5] The allure of this approach is that it provides a total endovascular solution and is readily available, and implantation techniques are familiar to most surgeons performing EVAR. In addition, this is a versatile technique that is applicable to elective and nonelective presentations for a variety of aortic diseases.

Supported by good short-term and midterm outcomes, chimney/periscope EVAR (chEVAR) has been reported to be a reasonable alternative to branched or fenestrated repair in selected patients.[6-8] However, despite generally promising results with this technique, reports documenting late adverse events have emerged, raising concerns about intermediate and long-term durability.[9-11] Importantly, questions surrounding device choice and subsequent risk of chimney occlusion, type Ia endoleak, and mortality remain unanswered.[12] To date, the ideal aortic and chimney stent combination to avoid these adverse outcomes has not been defined.

Therefore, the purpose of this analysis was to review subjects treated electively for juxtarenal and pararenal aortic disease from the worldwide collected experience for the PERformance of chImney technique for the treatment of Complex aortic pathoLogiES (PERICLES) registry to identify optimal device combinations through association with chimney stent occlusion, type Ia endoleak, and survival.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective analysis of the multicenter PERformance of chImney technique for the treatment of Complex aortic pathoLogiES (PERICLES) registry data
- **Take Home Message:** In the PERICLES registry, the risk of chimney graft occlusion and type Ia endoleak was similar for all combinations of balloon-expandable covered stents and endografts, but chimney graft occlusion increased by 1.8 for each additional stent used, and survival was decreased in patients with some endograft/chimney combinations.
- **Recommendation:** This study suggests that using more than one stent increases the risk of chimney graft occlusion by 1.8-fold and that some combinations of chimney grafts and endografts may have an impact on mortality, chimney graft occlusion, or incidence of type Ia endoleak.

METHODS

In accordance with the principles of the Declaration of Helsinki, all sites participating in the registry acquired local Institutional Review Board approval to collect, share, and analyze deidentified data. The need for consent of the patient was waived by each center's committee for the study of human subjects.

Patient cohort. A complete description of the PERICLES registry has previously been published.[13] This is a non-industry supported registry with 13 participating European (n = 9) and U.S. (n = 4) centers that contributed a total of 517 patients treated from 2008 to 2014. No investigator received financial incentive to conduct the analysis. Patients were offered chEVAR at each center after determination that they were at high risk for open surgery, typically because of unique combinations of anatomic, cardiac, pulmonary, and renal comorbidities. Device choice, degree of aortic/chimney stent oversizing, and chimney stent type were selected at the surgeon's discretion.

Study design. The purpose of the study was to explore the PERICLES registry[13] to identify patterns of device utilization and their association with clinical outcomes. To further understand which device combination comparisons would provide the most clinically impactful analysis, the most commonly used combinations in relatively uniform indications were explored. Specifically, because of variable indications and device heterogeneity among centers, robust statistical comparison of individual graft subtypes was feasible only in examining the most commonly used device combinations. Therefore, a retrospective review of the database focused on identification of electively treated patients with juxtarenal or suprarenal disease, which accounted for ~80% of all patients in the registry. Only elective presentations were included in the analysis, similar to the original manuscript from the registry.[13] Patients with aortic disease extending above the superior mesenteric artery but below the diaphragm (type IV thoracoabdominal aortic aneurysm [TAAA]) were also included, similar to the original description of the registry.[13]

However, Crawford extent I to III TAAAs[14] were excluded. Dissection, intramural hematoma, and embolic disease with embolic plaque at the origin of the left subclavian artery were excluded. In addition, patients with missing stent type or indication and those lacking follow-up beyond the index hospitalization were excluded. Additional details about the inclusion and exclusion criteria for the analysis are depicted in Fig 1.

Using this schema, 11 different aortic stent grafts were identified, including some thoracic devices that were implanted into prior open or endovascular infrarenal aneurysm repairs. Three different categories of chimney stents were recognized: balloon-expandable covered stent (BECS), self-expanding covered stent, and self-expanding bare-metal stent. Three distinct groups of the most frequently used aortic device combinations were identified (n = 398; 73% of the originally reported

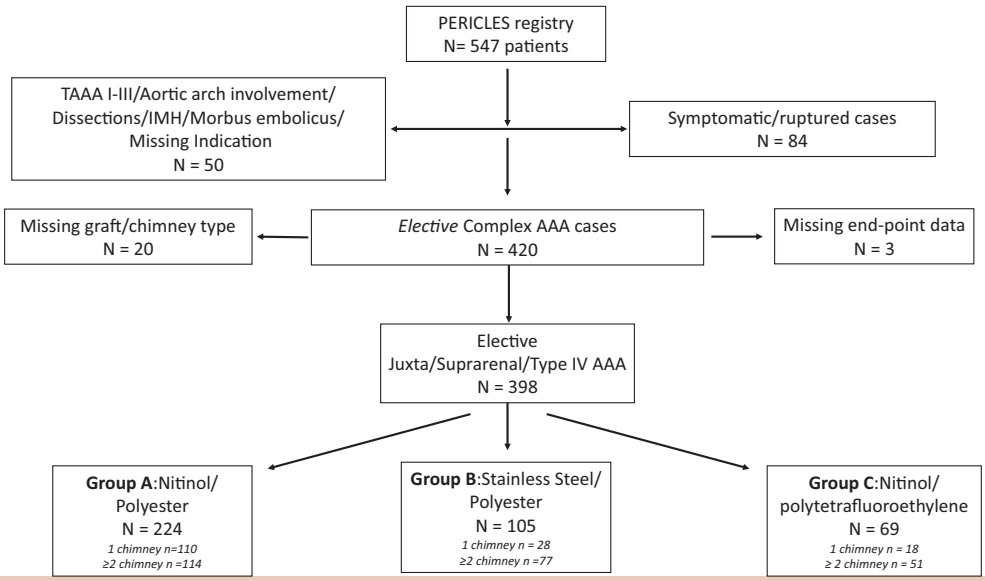

Fig 1. Inclusion and exclusion criteria. This diagram highlights the inclusion and exclusion criteria that were employed to define the study population within the PERformance of chImney technique for the treatment of Complex aortic pathoLogiES (*PERICLES*) registry. There were 398 patients for analysis who had the selected indications and data on chimney/aortic stent graft type as well as the end points of chimney occlusion, type Ia endoleak, and survival. The information on the number of chimney stents implanted (one vs two or more) for each aortic stent graft category is also included. *AAA*, Abdominal aortic aneurysm; *IMH*, intramural hematoma; *TAAA*, thoracoabdominal aortic aneurysm.

registry subjects[13]). In group A (n = 224), patients received an aortic nitinol/polyester stent graft, including Medtronic Endurant, Medtronic Endurant IIs, and Medtronic Talent (Medtronic, Santa Rosa, Calif) and AorFix (Lombard Medical, Irvine, Calif). In group B (n = 105), patients had a stainless steel/polyester stent including Cook Zenith, Cook Zenith Flex, and Cook TX2 (Cook Medical, Bloomington, Ind). In group C (n = 69), patients received nitinol/expanded polytetrafluoroethylene (NEP) aortic endografts, including Gore, Gore C3, and Gore TAG (W. L. Gore & Associates, Flagstaff, Ariz) and Ovation Prime (TriVascular, Santa Rosa, Calif).

Definitions. Juxtarenal aortic disease was defined as degenerative aneurysm extending to the level of the renal arteries. Additional categorization of juxtarenal aortic disease included type Ia endoleak after prior EVAR and para-anastomotic pseudoaneurysm after previous open repair. Suprarenal or pararenal aortic disease was defined by presence of aneurysmal dilation extending above the renal arteries but below the superior mesenteric artery. Demographics of the patients, comorbidities, and complications were recorded and categorized by the Society for Vascular Surgery reporting standards.[15] Endoleak was defined by recommended reporting guidelines.[15,16] Chimney patency was determined by follow-up computed tomography angiography.

End points and statistical analysis. The primary end point of the study was patient survival (time to event). Secondary end points included freedom from chimney occlusion (time to earliest event per graft) and intraoperative or late type Ia endoleak (probability of any occurrence at patient level). Descriptive statistics were used to characterize differences between device groups regarding demographics, comorbidities, and outcome variables. The Wilcoxon rank sum test, Pearson χ^2 (or Fisher exact) test, and log-rank test were used to univariately compare continuous, categorical, and time-to-event variables, respectively.

Multipredictor Cox proportional hazards regression[17] was used to assess relative differences in risk of chimney stent occlusion and overall mortality between patient groups defined by aortic endograft type (group A/B/C) and BECS use (yes/no). In the same regression model, we also considered the influence of treatment center volume (Udine and Münster, the highest volume centers, vs all others), use of internal lining chimney stent (yes/no), number of chimney stents/aortic endograft, number of chimney stent subtypes/aortic endograft (one vs more than one), and treatment center geographic location (European/non-European). To account for confounding of our effects of interest, we included additional predictors in the model (Table I) that were significantly associated with the outcome ($P < .05$) and that changed at least one estimated effect coefficient by at least 10% when included in the model. We used a variable clustering method[17] and variance inflation factors to assess collinearity among the predictors in the final models, removing any predictors with a variance inflation factor >2. We used a similarly composed multipredictor

Table I. Demographics of patients, comorbidities, indications, operative variables, and outcomes

Feature	Group A[a] (n = 224)	Group B[b] (n = 105)	Group C[c] (n = 69)	A = B = C *P* value[d]	A = (B or C) *P* value[d]
Age, years	76 (8)	74 (7)	76 (7)	.23	.91
Male	179 (86)	61 (75)	45 (74)	.03	.008
Comorbidities					
Hypertension	198 (88)	98 (93)	59 (86)	.21	.56
Dyslipidemia	132 (59)	78 (74)	38 (55)	.009	.11
Coronary artery disease	109 (49)	66 (63)	38 (55)	.05	.03
Chronic lung disease	85 (38)	48 (46)	26 (38)	.39	.37
Peripheral artery disease	37 (22)	7 (7)	19 (29)	.0002	.14
Congestive heart failure	79 (46)	15 (14)	27 (41)	<.0001	<.0001
Chronic renal insufficiency	99 (44)	52 (50)	37 (54)	.36	.18
Indication					
Juxtarenal AAA	176 (79)	48 (46)	46 (67)	<.0001	<.0001
Suprarenal AAA	39 (17)	54 (51)	17 (24)	—	—
Type IV TAAA	9 (4)	3 (3)	6 (9)	—	—
Preoperative AAA diameter, mm	61.0 (21.2)	63.3 (19.2)	66.4 (13.2)	.03	.44
Infrarenal neck diameter, mm	25.5 (4.2)	26.3 (4.5)	28.9 (6.1)	<.0001	<.0001
Infrarenal neck length, mm	4.7 (4.0)	4.1 (5.2)	2.6 (4.6)	<.0001	<.0001
Infrarenal neck calcification	35 (16)	4 (7)	14 (21)	.06	.64
Infrarenal neck thrombus	32 (15)	6 (11)	22 (33)	.002	.08
Suprarenal neck angle, degrees	22 (24)	25 (24)	15 (19)	.02	.53
Total chimney grafts	(n = 375)	(n = 208)	(n = 149)	—	—
Right renal artery	140 (37)	83 (40)	56 (38)	.007	.009
Left renal artery	175 (47)	81 (39)	59 (40)	—	—
Accessory renal artery	16 (4)	5 (2)	6 (4)	—	—
Superior mesenteric artery	41 (11)	35 (17)	18 (12)	—	—
Celiac artery	3 (1)	4 (2)	10 (7)	—	—
No, of stents/patient	1.7 (0.8)	2.2 (1.0)	2.0 (0.8)	<.0001	<.0001
Types of chimney grafts					
BECS	148 (66)	43 (41)	12 (17)	<.0001	<.0001
Self-expanding covered stent	60 (27)	39 (37)	56 (81)	<.0001	<.0001
Balloon-expandable metal stent	28 (13)	10 (10)	4 (6)	.23	.15
Endolining bare-metal stent	52 (23)	30 (29)	17 (25)	.58	.39
Intraoperative variables					
Operative time, minutes	217 (81)	255 (106)	249 (102)	.006	.002
Fluoroscopy time, minutes	50 (33)	58 (29)	86 (48)	<.0001	<.0001
Contrast material volume, mL	150 (47)	202 (83)	171 (66)	.002	.002
Type Ia endoleak	16 (7)	5 (5)	14 (20)	.003	.19
Outcomes					
30-Day mortality	5 (2)	2 (2)	2 (3)	.91	.98
Any mortality event	19 (9)	20 (19)	10 (15)	.01[e]	.005[e]
Any complication	12 (8)	20 (32)	10 (21)	<.0001	<.0001
Late type Ia endoleak	7 (5)	9 (9)	2 (3)	.29	.64
Treatment of type Ia endoleak	4 (6)	1 (2)	0	.19	.05
Any type Ia endoleak	21 (9)	13 (12)	14 (20)	.07	.06
Chimney occlusion	20 (11)	9 (11)	10 (16)	.72[e]	.50[e]

AAA, Abdominal aortic aneurysm; *BECS*, balloon-expandable covered stent; *TAAA*, thoracoabdominal aortic aneurysm.
Categorical variables are presented as number (%). Continuous variables are presented as mean (standard deviation).
[a]Group A: nitinol/polyester aortic endoskeleton.
[b]Group B: stainless steel/polyester aortic endoskeleton.
[c]Group C: nitinol/polytetrafluoroethylene (NEP) aortic endoskeleton.
[d]*P* values were estimated using the χ^2 test, Fisher exact test, or Kruskal-Wallis test.
[e]*P* values were estimated using the log-rank test.

logistic regression model[17] to assess simultaneous effects of the same factors on occurrence of intraoperative and late type Ia endoleak. We characterized relative differences in outcome risk by using model fits to estimate hazard ratios (HRs) or odds ratios (ORs) with 95% confidence limits and Wald test *P* values testing HR = 1 or OR = 1.

We also considered the need to account for variability in outcome risk among the 13 centers represented in our study sample. However, many of our effects of interest are structurally confounded with center. This is obviously the case for high-volume center status and European center status, but aortic endograft and BECS use are also strongly clustered within small numbers of centers. Among the six combinations of device group (A/B/C) and BECS use (yes/no), two to four centers (although not necessarily the same centers) accounted for 77% to 91% of all grafts placed for each combination. Because of the strong competition for between-center variability between many of our effects of interest and a center random effect that could be included in mixed effect versions of our models,[18] we decided to present results from models that did not account directly for between-center variability. However, we did fit these models and noted significant treatment center random effects for mortality and type Ia endoleak but not for chimney occlusion. We report the HR = 1 or OR = 1 *P* values from these mixed effect models for any of our estimated effects that were significant at .05 without the addition of the center random effect.

Finally, to provide a basis for interpreting nonsignificant HRs and ORs for device group comparisons (B:A, C:A) with or without BECS, we calculated minimum HRs and ORs that could be detected with 80% power at a two-sided significance level of .05. We used the study stratum sample sizes as well as observed occlusion and mortality hazard rates and endoleak proportions from group A in our calculations.[19] All statistical calculations were carried out using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Patient cohort. There were 398 patients identified with sufficient data on device combinations and outcomes. The three distinct aortic stent graft/chimney device combination populations were group A (n = 224), group B (n = 105), and group C (n = 69). Notably, a majority (55% [n = 148]) of patients received a nitinol/polyester stent graft aortic endoprosthesis (group A) and a BECS. Additional details about demographics, comorbidities, indications, and outcomes by subgroups are highlighted in Table I.

Risk of chimney occlusion. Based on study stratum sample sizes, we determined that a minimum occlusion HR of 2.3 could be detected with 80% power for both B:A and C:A device group comparisons when BECS was not employed. With BECS use, occlusion HRs of 2.1 and 3.1 could be detected with 80% power for B:A and C:A comparisons, respectively. The rate of any chimney occlusion across the three subgroups was 10% (39 of 398 patients).

In examining patients treated specifically with BECS, group B or C device combinations were associated with a 1.8-fold (HR, 1.8; 95% confidence interval [CI], 0.6-5.8; *P* = .33) higher risk of stent occlusion (Table II, *A*). Group C patients receiving BECS did have a trend toward higher occlusion risk relative to group C patients not receiving a BECS chimney stent (HR, 4.0; 95% CI, 0.85-18.84; *P* = .08). However, occlusion-free survival for patients receiving a BECS chimney stent was not significantly different when subjects were treated with either group A, B, or C devices (Cox model, *P* = .25; Fig 2, *A*). The 1- and 3-year freedom from chimney occlusion in comparing group A + BECS vs the composite group (B/C + BECS) was 96% ± 2% vs 93% ± 3% and 87% ± 5% vs 76% ± 10%, respectively (Fig 2, *B*). Notably, there was no significant effect of center volume on risk of chimney occlusion among patients treated with any chimney subtype/aortic stent combination (HR, 0.8; 95% CI, 0.3-2.0; *P* = .60). However, an increased number of chimney stents/aortic endografts, irrespective of chimney subtype, significantly increased risk of chimney occlusion (Cox model, *P* = .010; Fig 3, *A*; HR, 1.8 for each additional stent; 95% CI, 1.2-2.9; *P* = .01). Similarly, patients with an internal bare-metal stent used to support the chimney stent were also more likely to experience chimney occlusion (Cox model, *P* = .05; Fig 3, *B*).

Risk of type Ia endoleak. For intraoperative and late type Ia endoleaks, an OR of 3.2 could be detected for both B:A and C:A comparisons without BECS. ORs of 4.1 and 8.7 could be detected for B:A and C:A comparisons, respectively, when BECS was employed. Identification of any intraoperative type Ia endoleak occurred in 9% of the study cohort (35 of 398 patients). Of the 35 type Ia endoleaks, 51% (n=18) were noted in late, out of hospital postoperative imaging after the index chEVAR.

Aortic device group comparisons by subtype (BECS yes/no) are depicted in Table II, *B*. There were no significant differences in the rates of reported type Ia endoleak between groups, with or without use of BECS: 9%, 12%, and 20% for groups A, B, and C, respectively. Group C patients had higher risk of type Ia endoleak relative to groups A and B without a BECS chimney stent (C vs B, no BECS: OR, 3.2 [95% CI, 1-11; *P* = .05]; C vs A/B, no BECS: OR, 2.4 [95% CI, 0.9-6.4; *P* = .08]). The risk for development of any type Ia endoleak was substantially less when high-volume centers completed the chEVAR repair, without regard to aortic endograft/chimney

Table II. A, Hazard ratios (*HRs*) for risk of incident chimney stent occlusion

Scenario	Comparison	HR	95% CI	*P* value
No BECS used	Group B:group A	0.5	0.1-1.8	.27
	Group C:group A	0.6	0.2-1.7	.30
	Group B or C:group A	0.5	0.2-1.4	.20
BECS used	Group B:group A	1.5	0.4-5.5	.53
	Group C:group A	3.5	0.8-15.0	.10
	Group B or C:group A	1.8	0.6-5.8	.33
Group A	BECS yes:no	0.6	0.2-1.7	.36
Group B	BECS yes:no	2.0	0.5-8.4	.34
Group C	BECS yes:no	4.0	0.8-18.8	.08
Group B or C	BECS yes:no	2.2	0.7-6.5	.15
	Volume high:low	0.8	0.3-2.0	.60
	Internal lining chimney stent yes:no	2.1	1.0-4.5	.05
	Change in hazard rate for each additional chimney stent	1.8	1.2-2.9	.01
	1 chimney type:≥2 chimney types	0.5	0.1-1.9	.28
	European center yes:no	0.9	0.3-2.3	.81

BECS, Balloon-expandable stent; *CI,* confidence interval.
Group A, nitinol/polyester aortic endoskeleton; group B, stainless steel/polyester aortic endoskeleton; group C, nitinol/expanded polytetrafluroethylene (NEP) aortic endoskeleton.
Time to earliest chimney stent occlusion; all HRs are estimated from the same multipredictor Cox proportional hazards model and are adjusted for age, chronic heart failure, presence of type IV thoracoabdominal disease, preoperative neck thrombosis, and preoperative neck diameter.

Table II. B, Odds ratios (*ORs*) for risk of type Ia endoleak

Scenario	Comparison	OR	95% CI	*P* value[a]
No BECS used	Group B:group A	0.6	0.2-1.8	.35
	Group C:group A	1.9	0.6-5.4	.26
	Group B or C:group A	1.0	0.4-2.6	.99
BECS used	Group B:group A	0.8	0.2-2.8	.68
	Group C:group A	2.1	0.4-12.1	.39
	Group B or C:group A	1.0	0.3-3.1	.94
Group A	BECS yes:no	0.8	0.3-2.4	.72
Group B	BECS yes:no	1.1	0.3-4.3	.89
Group C	BECS yes:no	0.9	0.2-5.3	.95
Group B or C	BECS yes:no	0.8	0.3-2.3	.65
	Volume high:low	0.2	0.1-0.7	.01 (.16)
	Internal lining chimney stent yes:no	0.9	0.4-1.9	.74
	Change in odds for each additional chimney stent	0.6	0.3-1.0	.07
	1 chimney type:≥2 chimney types	2.1	0.7-6.7	.21
	European center yes:no	5.5	1.9-16.6	.002

BECS, Balloon-expandable stent; *CI,* confidence interval.
Group A, nitinol/polyester aortic endoskeleton; group B, stainless steel/polyester aortic endoskeleton; group C, nitinol/expanded polytetrafluoroethylene (NEP) aortic endoskeleton.
Any occurrence of intraoperative or late (postoperative or postdischarge) type Ia endoleak; all ORs are estimated from the same multipredictor logistic regression model and are adjusted for chronic heart failure, presence of suprarenal aortic disease, preoperative neck thrombosis, preoperative maximum aneurysm diameter, and need for chimney placement in the superior mesenteric artery.
[a]*P* value in parentheses is from a parallel model in which treatment center was modeled as a random effect (note that variability in outcome risk among treatment centers is structurally confounded with the effects of device group, BECS use, treatment center volume, and European center status).

subtype (OR, 0.2; 95% CI, 0.1-0.7; $P = .01$). Unlike chimney stent occlusion risk, where the risk of occlusion increased with increasing number of chimney stents employed per aortic endograft, use of multiple chimney stent combinations during the same repair was not significantly associated with greater risk for development of type Ia endoleak (change in OR for each additional chimney stent type: OR, 0.6; 95% CI, 0.3-1.0; $P = .07$).

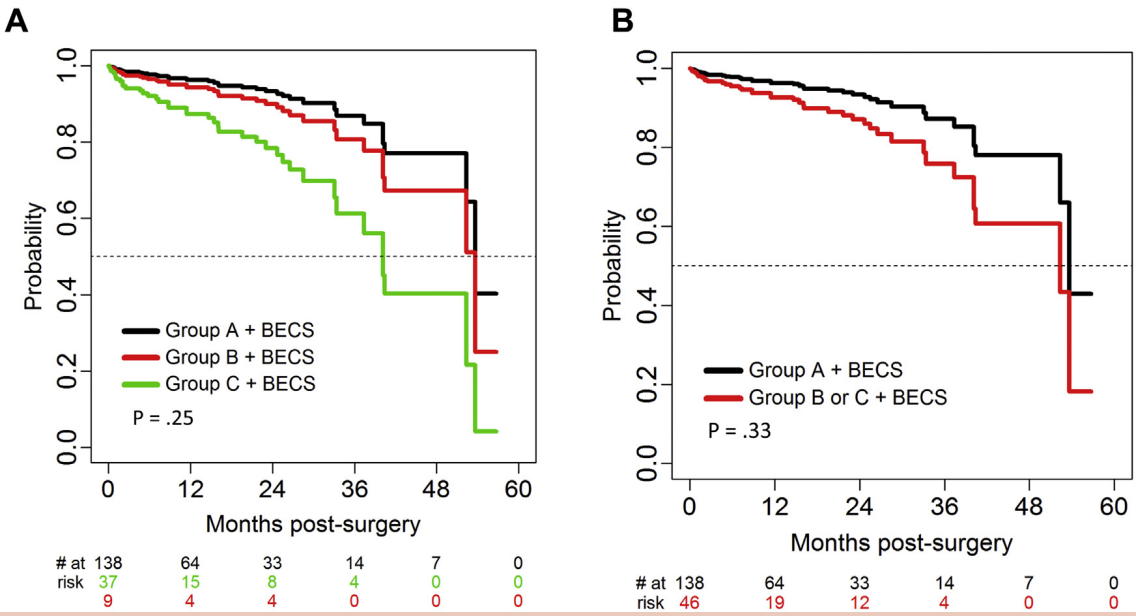

Fig 2. A, Occlusion-free survival of balloon-expandable covered chimney stents. This Cox regression model curve depicts the estimated occlusion-free survival for the three different groups that were analyzed. Comparison of patients treated with a nitinol/polyester endograft (group A) and a balloon-expandable covered stent (*BECS*) chimney stent graft with either a stainless steel/polyester (group B) or nitinol/expanded polytetrafluoroethylene (NEP) endoskeleton plus BECS revealed no significant difference in occlusion-free survival (Cox model, $P = .247$). No difference in chimney occlusion-free survival was present when a non-BECS chimney stent was used in conjunction with the three different aortic stent subtypes. **B,** Balloon-expandable covered chimney stent occlusion-free survival. Whereas the overall occlusion-free survival for all patients in the three different aortic stent graft groups was not different when a non-BECS chimney stent was employed, in examining patients managed *only* with BECS, no trend toward improved occlusion-free survival was noted in patients receiving a nitinol/polyester aortic endograft (group A) compared with the group treated with either a stainless steel/polyester (group B) or NEP (group C) endograft (Cox model, $P = .330$).

Mortality risk. Our stratum sample sizes allow a minimum mortality HR of 2.6 to be detected at 80% power for both B:A and C:A comparisons when BECS was not used. Mortality HRs of 3.0 and 4.4 could be detected for B:A and C:A comparisons, respectively, with use of BECS. There were 49 patients (12%) who died at some point during follow-up.

Among the analyzed device combinations, a significantly increased risk in mortality was detected in patients receiving a group C aortic endograft compared with group A when a BECS chimney stent was employed (HR, 5.3; 95% CI, 1.6-17.5; $P = .006$; Table III). However, no difference in survival was detected with other aortic/chimney stent combinations. The 1- and 3-year survival for group A + BECS vs group B/C + BECS was 97% ± 1% vs 90% ± 3% and 92% ± 3% vs 77% ± 7% (Cox model, $P = .02$; Fig 4), respectively. Notably, long-term mortality risk was 6.4 times higher (HR, 6.4; 95% CI, 1.7-24.8; $P = .007$) in group C patients receiving a BECS chimney stent compared with group C patients who did not receive a BECS. When two or more chimney stent subtypes were employed, the mortality risk was greater (HR, 3.2; 95% CI, 1.4-7.5; $P = .006$). Three-year survival was 90% ± 2% with use of a single chimney subtype vs 72% ± 10% in patients receiving multiple chimney subtypes (Cox model, $P = .006$; Fig 5).

DISCUSSION

This is the largest experience and first description to date examining which aortic endograft and chimney stent combinations are associated with development of postoperative chimney occlusion, type Ia endoleak, and mortality after chEVAR. Significant differences in these outcomes were identified in comparing various aortic/chimney stent combinations in the PERICLES registry. Notably, similar to descriptions of complex open aortic repair, an important volume-outcome relationship was detected in exploring rates of type Ia endoleak. The value of chEVAR is further demonstrated by excellent midterm survival. These findings provide important insights about what the optimal method is for performing chEVAR in elective patients with pararenal aortic disease.

Based on the results of this analysis, specific chimney stent subtype/aortic endograft combinations appeared to reduce risk of type Ia endoleak occurrence when a non-BECS chimney stent was employed (eg, group A/B vs C), but no difference in groups was noted when a BECS chimney stent was used. The most important

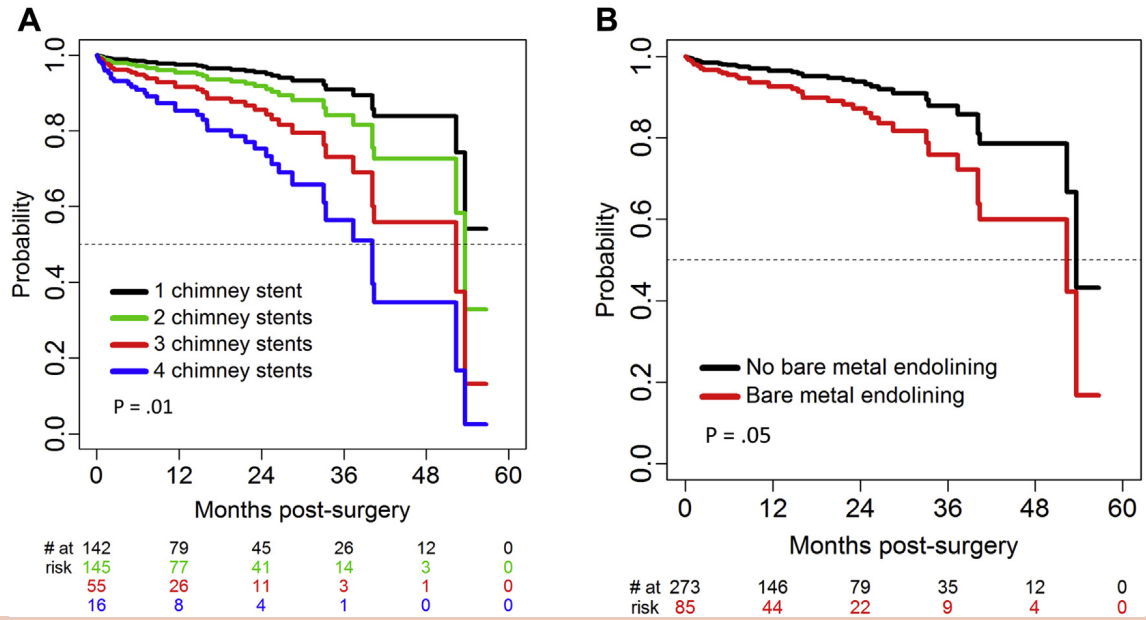

Fig 3. A, Any chimney subtype occlusion-free survival as a function of chimney number. A significant chimney occlusion-free survival advantage is noted in patients treated with a lower total number of chimney stents (Cox model, $P = .010$). The risk of increasing the number of chimney stents on likelihood for development of a chimney occlusion event in follow-up was 1.8-fold for each additional chimney stent (hazard ratio [HR], 1.8; 95% confidence interval [CI], 1.2-2.9; $P = .010$). **B,** Impact of a bare-metal stent lining any chimney stent subtype on occlusion-free survival. Irrespective of the chimney subtype (balloon-expandable covered stent [BECS], self-expandable covered, or bare-metal stent), if an internal bare-metal stent was added to the repair, this resulted in a significantly higher risk of chimney occlusion (HR, 2.1; 95% CI, 1.0-4.5; Cox model, $P = .05$).

factor in reducing type Ia endoleak risk was center volume. An important technical consideration in chEVAR is that a significant degree of device oversizing is necessary to allow the main aortic stent graft to conform around the chimney stent to prevent type Ia (gutter) endoleak.[20] However, if aortic devices are significantly oversized relative to the native aortic neck landing zone diameter, this may increase risk of chimney stent compression and subsequent occlusion and renal or visceral malperfusion.[11,21-24] The relative oversizing of endografts was left to the discretion of surgeons participating in the PERICLES registry, and specific information on this variable is not available.

Currently, there is a lack of prospective, multicenter randomized trial data to validate a specific chEVAR technique; however, multiple single-center studies have reported encouraging results with different approaches.[8,25-27] An important aspect of successful chEVAR is selection of an aortic device that conforms to the axial aortoiliac anatomy, providing fixation and minimizing type Ia endoleak while simultaneously permitting expansion of the renal/visceral chimney stent. The unique biomechanical properties of the various commercially available endografts will invariably interact differentially with the chimney stent and aortic wall.

A fundamental question is, What are the biomechanical properties of an ideal aortic and chimney stent configuration that will afford the best opportunity to harmonize the complex and dynamic hemodynamic environment after chEVAR? It is highly unlikely that randomized data will ever be available to definitively answer this question, but important outcome trends can be identified in examining this registry. For example, several factors may be related to the observation that an increasing number of chimney stents increased risk of occlusion or that multiple different chimney stent subtypes as well as repairs using NEP aortic grafts without a BECS were associated with increased mortality. Different aortic endograft/chimney stent configurations may allow enhanced vessel conformability and recoil control in selected anatomies, similar to results in the peripheral circulation with superficial femoral artery interventions.[28] Although speculative in chEVAR patients, these differences have been identified in other vascular beds, such as increased risk of stent collapse with stainless steel vs nitinol stents in the extracranial carotid circulation.[29] Moreover, there are dramatic loading forces imparted on the aortic endograft relative to shear forces, and the resulting stress hysteresis produces biased stiffness of the endoprosthesis favoring more resilient alloys.[30,31]

Unlike stainless steel, nitinol constructs have superior elasticity and can continue to exert a low outward radial force while resisting external compressive forces from a

Table III. Hazard ratios (*HRs*) for risk of incident overall mortality

Scenario	Comparison	HR	95% CI	*P* value[a]
No BECS used	Group B:group A	1.8	0.7-4.7	.21
	Group C:group A	0.7	0.2-2.3	.54
	Group B or C:group A	1.1	0.5-2.9	.79
BECS used	Group B:group A	2.1	0.7-6.6	.18
	Group C:group A	5.3	1.6-17.5	.006 (.99)
	Group B or C:group A	2.6	0.9-7.3	.07
Group A	BECS yes:no	0.8	0.3-2.2	.69
Group B	BECS yes:no	1.0	0.4-2.6	.94
Group C	BECS yes:no	6.4	1.7-24.8	.007 (.77)
Group B or C	BECS yes:no	1.9	0.8-4.4	.14
	Volume high:low	0.7	0.3-1.7	.44
	Internal lining chimney stent yes:no	1.0	0.5-2.0	.91
	Change in hazard rate for each additional chimney stent	0.7	0.4-1.1	.09
	1 chimney type:≥2 chimney types	3.2	1.4-7.5	.006
	European center yes:no	0.6	0.2-1.5	.26

BECS, Balloon-expandable stent; *CI*, confidence interval.
Group A, nitinol/polyester aortic endoskeleton; group B, stainless steel/polyester aortic endoskeleton; group C, nitinol/expanded polytetrafluoroethylene (NEP) aortic endoskeleton.
All HRs are estimated from the same multipredictor Cox proportional hazards model and are adjusted for chronic obstructive lung disease, presence of type IV thoracoabdominal disease, and preoperative maximum aneurysm diameter.
[a]*P* values in parentheses are from a parallel model in which treatment center was modeled as a random effect (note that variability in outcome risk among treatment centers is structurally confounded with the effects of device group, BECS use, treatment center volume, and European center status).

chimney stent (graft) and the native aortic wall.[30,31] Another possible reason for observed differences is that specific aortic endograft design features, such as nitinol/polyester constructs, may provide the ability to have tissue ingrowth with polyester as well as reduce the need for increased external supportive rings by the increased rigidity of the polyester fabric. In addition, there is an increased risk of fabric infolding with self-expanding expanded polytetrafluoroethylene stent grafts in the peripheral circulation with device oversizing,[32] which could theoretically increase risk of type Ia (gutter) endoleak.[33]

The observation in this study that an increasing number of chimney stents and use of internal chimney bare-metal endolining stents were associated with greater chimney occlusion risk is notable. Mechanistic understanding of why an increased number of chimney stent combinations may or may not confer risk of stent occlusion is lacking. In vitro studies have determined that optimal aortic device oversizing for chEVAR is ~30%, but there is significantly increased risk of gutter leak with an NEP stent graft and BECS.[33] However, this was not observed in this analysis.

Whereas there are no prospective in vivo data comparing multiple graft combinations during chEVAR, there are important interactions between the aorta, chimney stents, and abdominal branch vessels that likely have an impact on risk of chimney occlusion. For example, Ullery et al[23] quantified the respiratory-induced cyclic abdominal branch vessel deformation after chimney and fenestrated endografting. They demonstrated that renal arteries treated with chEVAR were forced into a downward, curved angle at the distal end of the stent and postulated this as a potential explanation for stent fracture and flow perturbation at this location. However, Sylvan et al[34] revealed no significant relationship between vessel curvature severity and branch occlusion, stenosis, or endoleaks after endovascular TAAA repair.

A unique contribution of this analysis is that it provides insight into an important volume effect on type Ia endoleak incidence. Similar to open juxtarenal and pararenal aortic disease management,[35] high-volume centers demonstrated better outcomes after chEVAR. Although speculative, the underlying reasons for this may be related to higher volume centers having improved selection of patients and greater appreciation of important technical considerations that may affect outcomes. These findings further support the concept of regionalizing complex aortic disease to high-volume centers.[36]

The most important determinant of successful aneurysm repair is survival of the patient. Patients who received an NEP + BECS endograft/chimney device combination had a distinct survival advantage compared with those receiving an NEP without a

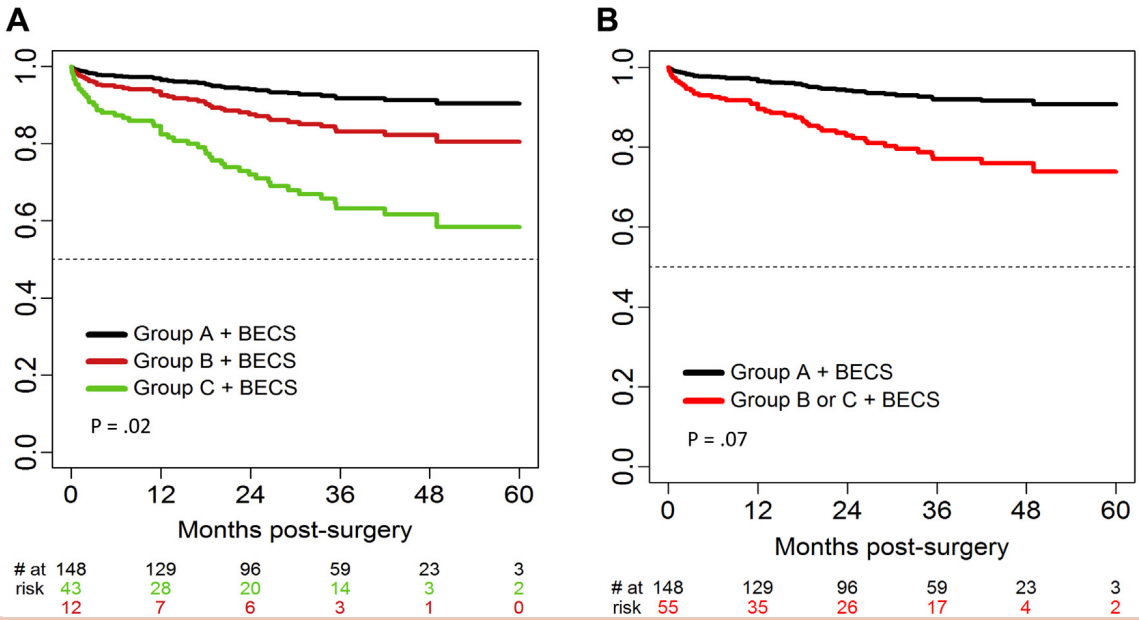

Fig 4. A, Overall patient survival for chimney endovascular aneurysm repair (chEVAR) with a balloon-expandable covered stent (*BECS*). Patients undergoing chEVAR with a nitinol/polyester aortic endograft (group A) with a BECS had significantly better survival compared with subjects receiving a BECS chimney stent with stainless steel/polyester (group B) or nitinol/polytetrafluoroethylene (NEP; group C) aortic stents (Cox model, $P = .024$). **B,** Overall patient survival after chEVAR using a BECS. Patients undergoing chEVAR that used a BECS had a trend ($P = .068$) toward being associated with improved survival by repair with a nitinol/polyester aortic endoprosthesis (group A) compared with subjects receiving a stainless steel/polyester (group B) or NEP (group C) aortic stent.

BECS chimney stent. This finding was observed after we employed statistical methods to reduce the impact of covariate imbalance and selection bias. The reason there is an apparent survival difference between repairs using NEP + BECS vs NEP without BECS is unclear because risk-adjusted comparisons of the other endograft subgroups with other BECS vs non-BECS chimney combinations did not demonstrate a difference in survival.

Limitations. Although this is the largest experience to date describing differences between aortic endograft and chimney stent device combinations, there are several limitations to consider. First, this was a retrospective analysis of a registry that captures self-reported data. We do not have prospective, randomized data that compare one aortic endograft and chimney stent type with other configurations to definitively answer what the best graft combination is for chEVAR. Furthermore, the number of observed events is small, and type II error is possible. The inherent selection bias that went into decisions about various device combinations cannot be fully accounted for and certainly had an impact on the results. In an attempt to address these shortcomings, we employed rigorous statistical methodology to better understand whether there were signals in the data that identified intragraft differences associated with specified end points.

Another limitation is that variability in outcome risk attributable to treatment centers is structurally confounded with the effects of device group, BECS use, center volume, and European center status. Because of this, we chose to present results without accounting for extra variability due to center, although we also report in our results tables how the significance of our results changes when center is modeled as a random effect. The final group of patients selected for the analysis accounts for only 73% of the cases in the originally reported registry. However, this was done intentionally because we made every effort to identify patients who were treated under relatively uniform conditions (eg, elective cases) for similar indications (eg, juxtarenal or pararenal aneurysm) and statistically controlled for between-center variation when possible. We do not know whether multiple chimney stents crossed one another and contributed to stent compression or aortic endograft displacement from the aortic wall. Similarly, we do not know how stent morphology or target vessel angulation changed over time, which could also contribute to these outcomes. We elected to analyze only chimney occlusion, type Ia endoleak, and mortality. Reintervention risk, branch vessel patency, and renal outcomes were not selected; however, this was due to the concept that we believe the most crucial outcomes defining successful chEVAR are encompassed by the end points described in our study.

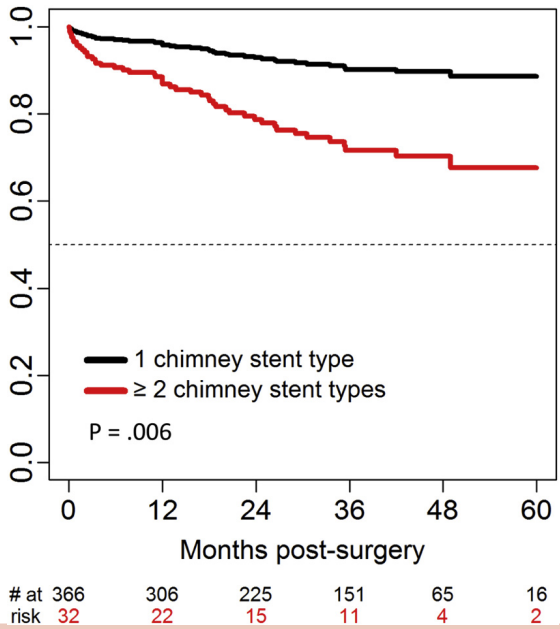

Fig 5. Overall patient survival as a function of the number of chimney stents implanted. Patients who had repair with a single chimney subtype had significantly better long-term survival compared with subjects undergoing repair with two or more chimney stent subtypes (Cox model, $P = .006$). This was independent of the specific aortic and chimney subtype that was used in the repair.

CONCLUSIONS

This analysis provides important insight into which device combinations used during chEVAR are associated with different outcomes in the PERICLES registry. Patients treated with any of the examined aortic stent graft designs in conjunction with various combinations of different chimney stent subtypes had no difference in risk of chimney occlusion. However, chimney occlusion risk is increased when a bare-metal self-expanding lining stent within a chimney stent or multiple chimney stents are used during the repair. Importantly, patients treated at low-volume centers have higher risk for development of type Ia endoleak. Poorer long-term survival occurs in subjects receiving certain different aortic endograft/chimney subtype combinations. These findings should inform clinicians considering chEVAR in the elective treatment of juxtarenal and pararenal aortic disease so that improved patient and device selection can occur to achieve optimal outcomes.

AUTHOR CONTRIBUTIONS

Conception and design: SS, KD
Analysis and interpretation: SS, AB, GT, ML, PK, FV, JL, KD
Data collection: SS, AB, GT, ML, PK, FV, JL, KD
Writing the article: SS, AB, PK, KD
Critical revision of the article: SS, AB, GT, ML, PK, FV, JL, KD
Final approval of the article: SS, AB, GT, ML, PK, FV, JL, KD
Statistical analysis: PK
Obtained funding: SS
Overall responsibility: SS
SS and AB contributed equally to this article and share first authorship.

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APPENDIX.

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