Influence of severe neck angulation on hemodynamic and clinical outcomes following endovascular aneurysm repair: a hemodynamic analysis and a retrospective cohort study

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Abstract

Background: For patients with severe neck angulation (SNA), hemodynamic and clinical outcomes following endovascular aneurysm repair (EVAR) are still unclear. This study aimed to explore the influence of SNA on hemodynamic and clinical outcomes following EVAR.

Methods: This study included a hemodynamic analysis and a retrospective cohort study from West China Hospital of Sichuan University between January 2011 and December 2020. The Cox regression model, inverse probability of treatment weighting (IPTW) analysis, sensitivity analysis, and subgroup analysis were applied. Primary outcome was type IA endoleak (T1AEL).

Results: In this hemodynamic analysis, nine non-severe neck angulation (nSNA) and 16 SNA idealized models were constructed. We found a significant difference in drag force between SNA and nSNA models (7.016 ± 2.579 N *vs*. 4.283 ± 1.460 N, $P = 0.008$), and proximal neck angles were significantly associated with the magnitude of drag force ($F = 0.082 \times \alpha - 0.006 \times \beta + 2.818$, α: 95% confidence interval [CI] 0.070–0.094; $P = 0.001$; β: 95% CI −0.019 to 0.007; $P = 0.319$). In our cohort study, 514 nSNA patients (71.5 ± 8.5 years; 459 males) and 208 SNA patients (72.5 ± 7.8 years; 135 males) were included, with a median follow-up duration of 34 months (16–63 months). All baseline characteristics were well balanced after IPTW matching. We found that SNA was associated with a significant risk of adverse limb event (hazard ratio [HR] 2.18, 95% CI 1.09–3.12), yet was not associated with T1AEL, overall survival, or reintervention. In patients without proximal or distal additional procedures (DAP), subgroup analyses suggested a significant risk of T1AEL (Proximal: HR 5.25, 95% CI 1.51–18.23; Distal: HR 5.07, 95% CI 1.60–16.07) and adverse limb event (Proximal: HR 2.27, 95% CI 1.01–5.07; Distal: HR 2.91, 95% CI 1.30–6.54) in SNA patients. However, no noticeable difference was observed in patients with proximal or DAP.

Conclusions: SNA has a critical influence on hemodynamic and clinical outcomes following EVAR. Appropriate additional procedures may be of great benefit to SNA patients.

Keywords: Severe neck angulation; Endovascular aneurysm repair; Abdominal aortic aneurysm; Treatment outcome; Hemodynamics

Introduction

Endovascular aneurysm repair (EVAR) has been accepted worldwide to treat infrarenal abdominal aortic aneurysm (AAA) for anatomically suitable patients.[1,2] However, clinical outcomes in patients with hostile necks, such as severe neck angulation (SNA), are still under debate. With older generation stent–grafts, SNA is considered outside the instructions for use (IFU) and is associated with type I endoleak, reintervention, and late sac expansion.[3-5] With the introduction of technological advances over the last 2 decades, newer generation stent–grafts have yielded better performance at early to mid-term outcomes in SNA patients.[6-8] However, the small sample sizes and mixed devices limit the influence of SNA on clinical outcomes following EVAR.

Meanwhile, computational fluid dynamics (CFD) is a new research technique used to investigate the mechanics of stent–graft positional stability by reconstructing a three-dimensional model of the AAAs and stent–grafts.[9-11] The magnitude and direction of the drag force is a critical factor in stent–graft performance. Previous studies on the relationship between drag force and suprarenal neck angle revealed that the suprarenal neck angle and the magnitude of drag force had a significant association.[12,13] However,

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the influence of infrarenal neck angle and SNA on hemodynamic outcomes following EVAR is still unclear.

Therefore, the current study aimed to explore the influence of SNA on hemodynamic outcomes using CFD and to analyze the influence of SNA on clinical outcomes at a high-volume hospital in China.

Methods

Ethical approval

This study was approved by the Institutional Review Board of West China Hospital (No. 2019-823). Patient consent was waived due to the anonymization of the data.

Study design

This study consisted of a hemodynamic analysis and a retrospective cohort study. The observational study was performed according to the guidelines of Strengthening the Reporting of Observational Studies in Epidemiology [Supplementary Table 1, http://links.lww.com/CM9/B266].[14]

Patient population

All verified AAA patients who underwent EVARs from January 2011 to December 2020 at West China Hospital of Sichuan University were included. Exclusion criteria included: abdominal pseudoaneurysms or dissections; chimney, fenestrated, or branched stent–grafts; reinterventions; AAAs with short necks (<10 mm); and inadequate imaging examinations. All EVAR procedures were performed by the same team in a hybrid operating room. Only Endurant or Endurant II stent–grafts (Medtronic, Santa Rosa, CA, USA) were implanted. Included patients were classified into a SNA group and a non-severe neck angulation (nSNA) group according to the proximal neck anatomy before operation. For neck length >15 mm, SNA was defined as an infrarenal angle (β) >75° and/or a suprarenal angle (α) >60°, or β >60° and/or α >45° for a neck length of 10–15 mm, according to the IFU of this stent–graft.[6,15,16]

Follow-up and outcomes

For all patients, duplex ultrasound (DUS) was regularly started at 1, 3, 6, and 12 months after discharge, and annually thereafter. If any EVAR-specific adverse events occurred,[17] computed tomography angiography (CTA) was performed to obtain a better assessment. Moreover, phone calls were adopted to trace survival status if patients could not make it to outpatient clinics. Primary outcome was type IA endoleak (T1AEL). Secondary outcomes were adverse limb event (defined as type IB endoleak [T1BEL], type III endoleak [T3EL], and limb occlusion), overall survival, and reintervention.

Angulation measurements

Two independent researchers measured neck angulation according to a standardized and validated method introduced by van Keulen *et al*[6,18] Briefly, we first performed the center lume line (CLL) reconstruction using tridimensional imaging of the aorta, then rotated the aorta along its CLL axis until the sharpest angle was found, and measured the neck angulation, including both α and β angles. The details of the angulation measurements are presented in Supplementary File 1 and Supplementary Figure 1, http://links.lww.com/CM9/B266.

Covariates

Two independent investigators recorded the following baseline characteristics to reduce potential confounding effects: demographic covariates (including age, gender, body mass index, smoking status, and alcohol consumption); comorbidities (including hypertension, diabetes mellitus, chronic obstructive pulmonary disease [COPD], cardiac artery disease [CAD], and stroke); anatomical covariates (including neck diameter, neck length, neck angulation, neck oversizing ratio [OSR], aneurysm diameter, bilateral limb OSR, and ruptured AAA); and anesthetic techniques. The OSR was calculated as follows: the difference of diameter between the stent–graft and the native artery divided by the diameter of the native artery in the attachment zone. Additionally, we recorded the proximal additional procedure (PAP), which included the proximal neck dilation and the implantation of the covered cuff stent, and the distal additional procedure (DAP), which included the distal neck dilation and the limb extension to the external iliac artery.

CFD analyses

We designed 25 idealized models with different proximal neck angles 1 year post-EVAR. Preoperative α angles were set as 0°, 30°, 60°, 90°, and 120°, and β angles as 0°, 45°, 75°, 90°, and 120°. The corresponding α angles and β angles at 1 year post-EVAR were studied among 48 patients with preoperative and postoperative CTAs. The inlet for the model was the abdominal aorta 10 mm above the celiac trunk, and the input velocity was set as 0.26 m/s.[19] The outlets were the celiac trunk, the superior mesenteric artery, the bilateral renal arteries, and the bilateral limbs. The pressure of each outlet was set at 122 mmHg.[9,20] The finite volume method was implemented for CFD analyses to solve the Navier–Stokes equations, and the SIMPLE algorithm was used to solve the pressure velocity coupling in the ANSYS FLUENT software (v14.5, ANSYS Inc., Canonsburg, PA, USA). The drag force of the stent–graft — the primary outcome of the CFD analyses — was the total impact force of blood flow on the stent–graft and computed from the surface integration of pressure and wall shear stress.[9,12] The details of the CFD procedures are presented in Supplementary File 2 and Supplementary Figure 2, http://links.lww.com/CM9/B266.

Statistical analyses

For CFD analyses, scatter plots and linear regression were applied to explore the relationship between preoperative neck angles and the corresponding postoperative angles. Student's *t*-test was used to compare the drag force between the SNA and nSNA groups, and multiple linear regression analysis was used to explore the influence of α and β angles on the magnitude of drag force.

For clinical analyses, the sample size for the primary outcome T1AEL was calculated based on a ratio of nSNA group to SNA group of 2:1. Assuming a two-tailed type I error rate of 5%, a sample size of 618 was needed to give a >80% chance of detecting an increase in the incidence of T1AEL from 1.9% in the nSNA group to 6.5% in the SNA group.[4] Continuous variables were presented as mean and standard deviations (SDs) and analyzed with the Student's *t*-test; categorical variables were presented as absolute and relative percentages and analyzed with the Pearson χ^2 test or Fisher's exact test. Kaplan-Meier curves were used to compare time-to-event outcomes. To adjust for potential confounding factors, Cox proportional-hazards regression models were performed on baseline characteristics that showed a significant impact on univariate analysis ($P < 0.10$) or that were considered clinically relevant. Hazard ratios (HR) and 95% confidence intervals (95% CI) were estimated for the overall population and subgroup populations, separately for patients with PAPs and DAPs.

We also applied inverse probability of treatment weighting (IPTW), a propensity score method, to further balance the group differences in baseline characteristics.[21] Stabilized inverse probability weights were used to mitigate the influence of minimal probabilities estimated from the propensity score model.[22] Propensity scores were calculated via logistic regression for both groups considering 18 demographic, comorbidity, and anatomical covariates and using multiple imputations for missing covariate data.[23-26] Standardized differences of those included covariates were evaluated and compared before and after weighting, with a value of <10% indicating a good balance between groups. Moreover, the differences of included covariates between groups after IPTW were calculated by a weighted linear regression model. Sensitivity analysis was performed by using truncated weights with a specified threshold of the 1st and 99th percentiles of the propensity score distributions.[27]

Statistical significance was defined as a P value <0.05 and/or 95% CI. R studio (https://www.r-project.org, The R Foundation) and Empower (R) (www.empowerstats.com, X&Y Solutions, Inc., Boston, MA, USA) were used for all statistical analyses.

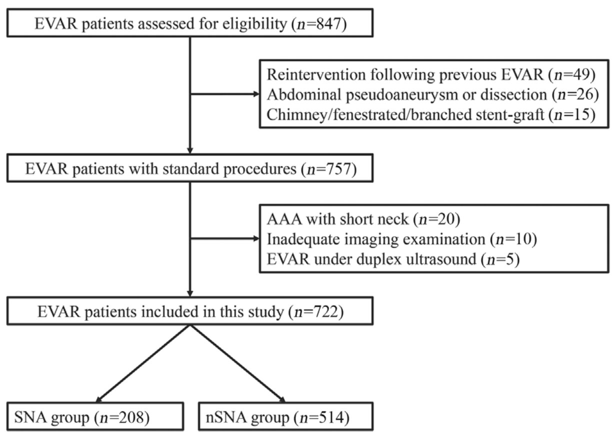

Figure 1: STROBE flow diagram of patient selection. EVAR: Endovascular aneurysm repair; nSNA: Non-severe neck angulation; AAA: abdominal aortic aneurysm; SNA: Severe neck angulation; STROBE: Strengthening the reporting of observational studies in epidemiology.

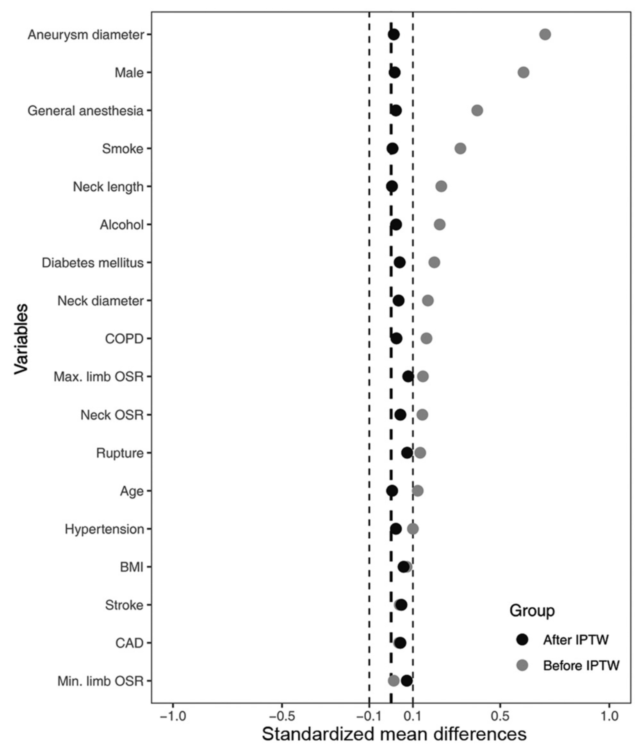

Figure 2: Standardized mean differences for all variables comparing the full unmatched cohort with the IPTW cohort. BMI: Body mass index; CAD: Cardiac artery disease; COPD: Chronic obstructive pulmonary disease; IPTW: Inverse probability of treatment weighting; Max.: Maximum value; Min.: Minimum value; nSNA: Non-severe neck angulation; OSR: Oversizing ratio; SMD: Standardized mean difference; SNA: Severe neck angulation.

Results

Patient characteristics before and after IPTW matching

A total of 722 patients were enrolled in this retrospective study [Figure 1], including 514 nSNA patients (mean [SD] age, 71.5 [8.5] years; 459 [89.3%] male) and 208 SNA patients (mean [SD] age, 72.5 [7.8] years; 135 [64.9%] male). The baseline characteristics of the two groups were different with regard to gender, smoking status, alcohol consumption, diabetes mellitus, COPD, neck diameter, neck length, aneurysm diameter, and anesthetic techniques. After IPTW matching, all covariates were well balanced with standardized differences <10% and P values >0.05 [Figure 2]. Patient baseline characteristics before and after IPTW matching are outlined in Table 1.

Hemodynamic outcomes

We enrolled 48 patients with both preoperative and postoperative CTA after 1 year. The results of scatter plot and linear regression analysis indicated there was a linear regression relationship between the preoperative and postoperative angles after 1 year [Figure 3], and the regression equations were listed as follows: $\alpha 2 = 0.668 \times \alpha 1 + 3.026$, $P < 0.001$; $\beta 2 = 0.617 \times \beta 1 + 3.627$, $P < 0.001$. Considering the pre-set preoperative α

Table 1: EVAR patients baseline characteristics before and after IPTW.

Variables	Before IPTW nSNA, $n=514$	Before IPTW SNA, $n=208$	SMD	t / χ^2	P value	After IPTW nSNA, $n=514$	After IPTW SNA, $n=208$	SMD	t / χ^2	P-value
Continuous data*										
Age (years)	71.5 ± 8.5	72.5 ± 7.8	0.122	−1.458	0.145	71.8 ± 8.8	71.8 ± 8.0	0.005	−0.061	0.952
BMI (kg/m^2)	23.3 ± 3.7	23.1 ± 3.6	0.071	1.072	0.495	23.3 ± 3.7	23.5 ± 3.6	0.057	−0.751	0.541
Neck diameter (mm)	21.4 ± 2.7	20.9 ± 2.6	0.168	2.031	0.043	21.3 ± 2.6	21.4 ± 2.8	0.034	0.458	0.647
Neck OSR	0.2 ± 0.1	0.2 ± 0.1	0.143	−1.758	0.079	0.2 ± 0.1	0.2 ± 0.1	0.042	−0.564	0.573
α angle (degree)	22.3 ± 16.8	62.9 ± 28.6	1.734	−23.685	<0.001	23.6 ± 16.8	58.1 ± 27.7	1.504	20.209	<0.001
β angle (degree)	36.8 ± 19.8	82.2 ± 24.4	2.047	−26.081	<0.001	37.8 ± 20.2	80.5 ± 22.6	1.991	26.738	<0.001
Neck length (mm)	29.4 ± 12.4	26.6 ± 11.7	0.230	2.772	0.006	28.4 ± 12.0	28.5 ± 12.4	0.004	0.055	0.956
Aneurysm diameter (mm)	51.8 ± 12.9	61.8 ± 15.1	0.706	−8.895	<0.001	55.4 ± 16.0	55.2 ± 13.5	0.012	−0.155	0.877
Max. limb OSR	0.2 ± 0.1	0.1 ± 0.1	0.146	1.760	0.079	0.1 ± 0.1	0.2 ± 0.1	0.078	1.048	0.295
Min. limb OSR	0.1 ± 0.1	0.1 ± 0.1	0.012	−0.149	0.882	0.1 ± 0.1	0.1 ± 0.1	0.072	0.973	0.331
Categorical data†										
Male	459 (89.3)	135 (64.9)	0.607	60.422	<0.001	82.20	82.80	0.016	−0.209	0.834
Smoke	325 (63.2)	99 (47.6)	0.318	14.931	<0.001	58.50	58.80	0.006	0.086	0.931
Alcohol	167 (32.5)	47 (22.6)	0.223	6.951	0.008	29.20	28.20	0.023	−0.310	0.756
Hypertension	360 (70.0)	136 (65.4)	0.100	1.492	0.222	68.90	70.00	0.022	0.301	0.763
Diabetes mellitus	74 (14.4)	17 (8.2)	0.198	5.207	0.022	12.70	11.50	0.039	−0.525	0.599
COPD	92 (17.9)	51 (24.5)	0.162	4.086	0.043	19.80	20.70	0.024	0.328	0.743
Stroke	32 (6.2)	15 (7.2)	0.039	0.236	0.627	6.30	5.200	0.047	−0.637	0.524
CAD	96 (18.7)	36 (17.3)	0.036	0.186	0.666	17.80	16.20	0.042	−0.560	0.575
General anesthesia	113 (22.0)	83 (39.9)	0.395	24.042	<0.001	27.60	26.60	0.022	−0.293	0.769
Rupture	56 (10.9)	32 (15.4)	0.133	2.789	0.095	12.20	14.70	0.073	0.979	0.327

* Continuous data presented as mean ± SD. † Categorical data presented as number (%). EVAR: Endovascular aneurysm repair; BMI: Body mass index; CAD: Cardiac artery disease; COPD: Chronic obstructive pulmonary disease; IPTW: Inverse probability of treatment weighting; Max., Maximum value; Min., Minimum value; nSNA: Non-severe neck angulation; OSR: Oversizing ratio; SD: Standard deviation; SMD: Standardized mean difference; SNA: Severe neck angulation.

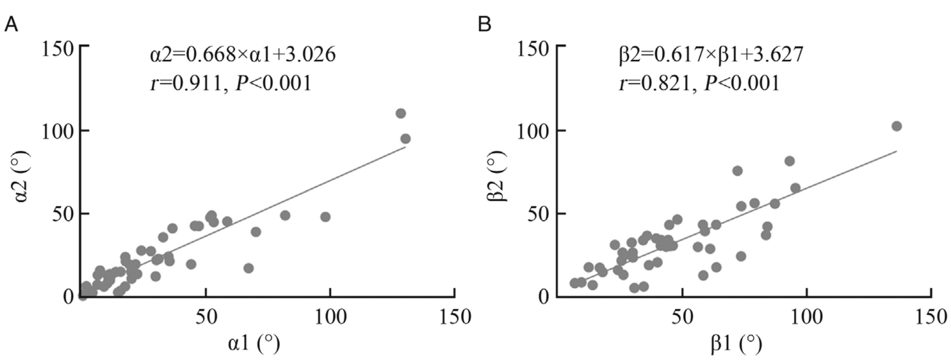

Figure 3: Scatter plots of the preoperative and postoperative angles 1 year after EVAR (A. α angle; B. β angle). EVAR: Endovascular aneurysm repair.

and β angles, the corresponding α angles at 1 year were set as follows: 0°, 23°, 43°, 63°, and 83°; and β angles: 0°, 31°, 50°, 59°, and 78°. Finally, we constructed 25 idealized models 1 year post-EVAR, consisting of 16 SNA and 9 nSNA models [Supplementary Figure 3, http://links.lww.com/CM9/B266]. After completing the CFD analyses, we found a significant difference in drag force between SNA and nSNA models (7.016 ± 2.579 N *vs.* 4.283 ± 1.460 N, $P = 0.008$) [Supplementary Table 2 and Supplementary Figure 4, http://links.lww.com/CM9/B266]. Multiple linear regression analysis revealed that the proximal neck angles were significantly associated with the magnitude of drag force ($F = 0.082 \times \alpha - 0.006 \times \beta + 2.818$, α: 95% CI 0.070–0.094; $P < 0.001$; β: 95% CI −0.019 to 0.007; $P = 0.319$).

Clinical outcomes

T1AEL

The median imaging follow-up after EVAR was 14 months (5–35 months), and 28 (3.9%) patients were lost to imaging follow-up due to the absence of any DUS or CTA examinations. The details of clinical events are shown in Table 2. A total of 20 (2.9%) patients suffered from T1AEL during follow-up, with 10 (2.0%) patients in the nSNA group and 10 (5.1%) in the SNA group. No significant difference between the groups was observed in the four analysis models in the whole cohort. In patients with PAPs or DAPs, there was also no significant association between SNA and T1AEL. However, in patients without PAPs, the results of subgroup analyses suggested that SNA was associated with a significant risk of T1AEL: in unadjusted analysis (HR 4.18, 95% CI 1.43–12.20); in the Cox model (HR 4.65, 95% CI 1.47–14.75); in IPTW analysis (HR 5.25, 95% CI 1.51–18.23); and in IPTW sensitivity analysis (HR 5.90, 95% CI 1.77–19.74). Similarly, in patients without DAPs, a significant risk of T1AEL was also obtained: in unadjusted analysis (HR 3.20, 95% CI 1.07–9.58); in the Cox model (HR 4.05, 95% CI 1.15–14.33); in IPTW analysis (HR 5.07, 95% CI 1.60–16.07); and in IPTW sensitivity analysis (HR 5.16, 95% CI 1.64–16.25) [Table 3].

Table 2: Clinical events in nSNA and SNA patients during follow-up.

Variables	Total, $n=722$	nSNA, $n=514$	SNA, $n=208$
Imaging follow-up time (months)*	14 (5–35)	14 (5–33)	14 (5–39)
T1AEL†	20/694 (2.9)	10/498 (2.0)	10/196 (5.1)
T1BEL†	35/694 (5.0)	17/498 (3.4)	18/196 (9.2)
T2EL†	124/694 (17.9)	79/498 (15.9)	45/196 (23.0)
T3EL†	9/694 (1.3)	4/498 (0.8)	5/196 (2.6)
Limb occlusion†	21/694 (3.0)	14/498 (2.8)	7/196 (3.6)
Adverse limb event†	60/694 (8.7)	35/498 (7.0)	25/196 (12.8)
Survival follow-up time (months)*	34 (16–63)	33 (16–62)	40 (16–66)
Reintervention†	45/711 (6.3)	25/508 (4.9)	20/203 (9.9)
Overall survival†	117/711 (16.5)	80/508 (15.8)	37/203 (18.2)

* Data presented as median (interquartile range). † Data presented as number/total (percentage). nSNA: Non-severe neck angulation; SNA: Severe neck angulation; T1AEL: Type IA endoleak; T1BEL: Type IB endoleak; T2EL: Type II endoleak; T3EL: Type III endoleak.

Table 3: Comparison of the clinical outcomes between SNA and nSNA in the unadjusted, COX, IPTW, and IPTW sensitivity analysis.

Outcomes	Number of patients	Unadjusted analysis HR (95% CI)	Cox model HR (95% CI)	IPTW analysis HR (95% CI)	IPTW sensitivity Analysis HR (95% CI)
T1AEL					
Total	694	2.35 (0.97–5.67)	2.09 (0.81–5.38)	2.44 (0.88–6.71)	2.68 (1.00–7.17)
PAP-yes	144	0.37 (0.07–2.06)	0.14 (0.02–1.06)	0.23 (0.04–1.19)	0.23 (0.04–1.19)
PAP-no	550	4.18 (1.43–12.20)	4.65 (1.47–14.75)	5.25 (1.51–18.23)	5.90 (1.77–19.74)
DAP-yes	196	1.04 (0.23–4.69)	0.74 (0.16–3.44)	0.65 (0.14–3.14)	0.95 (0.23–3.96)
DAP-no	498	3.20 (1.07–9.58)	4.05 (1.15–14.33)	5.07 (1.60–16.07)	5.16 (1.64–16.25)
Adverse limb event					
Total	694	1.66 (0.99–2.77)	1.84 (1.09–3.12)	2.18 (1.07–4.43)	1.88 (1.04–3.38)
PAP-yes	144	1.51 (0.36–6.38)	2.35 (0.50–11.08)	2.31 (0.52–10.26)	2.31 (0.52–10.26)
PAP-no	550	1.80 (1.02–3.18)	1.83 (1.01–3.32)	2.27 (1.01–5.07)	1.91 (1.01–3.61)
DAP-yes	196	1.27 (0.51–3.13)	1.20 (0.41–3.52)	0.72 (0.24–2.18)	1.19 (0.47–3.02)
DAP-no	498	1.72 (0.91–3.22)	1.54 (0.64–3.67)	2.91 (1.30–6.54)	2.12 (1.05–4.29)
T2EL					
Total	694	1.39 (0.96–2.01)	1.36 (0.94–1.97)	1.42 (0.91–2.23)	1.43 (0.93–2.20)
PAP-yes	144	1.06 (0.47–2.39)	0.95 (0.42–2.19)	0.90 (0.38–2.15)	0.90 (0.38–2.15)
PAP-no	550	1.50 (0.99–2.30)	1.51 (0.98–2.31)	1.59 (0.95–2.66)	1.62 (1.00–2.64)
DAP-yes	196	1.78 (0.94–3.37)	1.61 (0.83–3.13)	1.34 (0.60–3.01)	1.23 (0.63–2.44)
DAP-no	498	1.18 (0.74–1.88)	1.22 (0.76–1.95)	1.42 (0.84–2.40)	1.49 (0.88–2.53)
Reintervention					
Total	711	1.92 (1.07–3.47)	1.59 (0.86–2.97)	1.49 (0.71–3.14)	1.95 (0.96–3.96)
PAP-yes	152	0.49 (0.14–1.76)	0.40 (0.10–1.57)	0.30 (0.08–1.09)	0.31 (0.09–1.12)
PAP-no	559	2.82 (1.45–5.51)	2.30 (1.13–4.65)	2.10 (0.89–4.92)	3.07 (1.40–6.71)
DAP-yes	203	1.89 (0.74–4.81)	1.60 (0.56–4.56)	1.32 (0.44–3.93)	1.79 (0.66–4.91)
DAP-no	508	1.74 (0.79–3.86)	1.52 (0.67–3.46)	1.53 (0.57–4.10)	2.08 (0.81–5.34)
Survival					
Total	711	1.04 (0.71–1.54)	0.79 (0.51–1.24)	0.85 (0.51–1.42)	0.89 (0.56–1.43)
PAP-yes	152	0.59 (0.31–1.14)	0.49 (0.22–1.07)	0.75 (0.33–1.71)	0.56 (0.25–1.24)
PAP-no	559	1.09 (0.66–1.80)	0.96 (0.55–1.68)	0.74 (0.39–1.39)	0.94 (0.52–1.71)
DAP-yes	203	0.77 (0.41–1.46)	0.61 (0.28–1.29)	0.94 (0.42–2.11)	0.84 (0.40–1.78)
DAP-no	508	1.13 (0.69–1.85)	0.95 (0.54–1.66)	0.76 (0.41–1.40)	0.90 (0.50–1.61)

CI: Confidence interval; DAP: Distal additional procedure; HR: Hazard ratio; IPTW: Inverse probability of treatment weighting; nSNA: Non-severe neck angulation; PAP: Proximal additional procedure; SNA: Severe neck angulation; T1AEL: Type IA endoleak; T2EL: Type II endoleak.

Adverse limb event

The overall rate of post-EVAR adverse limb events was 8.7% (60/694), with respective rates of 7.0% (35/498) and 12.8% (25/196) in the nSNA and SNA groups. More specifically, there were 17 T1BELs, 4 T3ELs, and 14 limb occlusions in the nSNA group. Meanwhile, there were 18 T1BELs, 5 T3BELs, and 7 limb occlusions in the SNA group. We found that SNA was associated with a significant risk of adverse limb event: in the Cox model (HR 1.84, 95% CI 1.09–3.12); in IPTW analysis (HR 2.18, 95% CI 1.07–4.43); and in IPTW sensitivity analysis (HR 1.88, 95% CI 1.04–3.38). In patients without PAPs, we also found there was a significant association between SNA and adverse limb event: in unadjusted analysis (HR 1.80, 95% CI 1.02–3.18); in the Cox model (HR 1.83, 95% CI 1.01–3.32); in IPTW analysis (HR 2.27, 95% CI 1.01–5.07); and in IPTW sensitivity analysis (HR 1.91, 95% CI 1.01–3.61). At the same time, subgroup analyses in patients without DAPs yielded similar results in IPTW analysis (HR 2.91, 95% CI 1.30–6.54) and IPTW sensitivity analysis (HR 2.12, 95% CI 1.05–4.29). However, no obvious differences between the two groups were observed in patients with PAPs or DAPs [Table 3].

Overall survival and reintervention

The median follow-up was 34 months (16–63 months), and 11 (1.48%) patients were lost to follow-up for survival status. A total of 117 (16.5%) patients died and 45 (6.3%) underwent reintervention during follow-up. As for overall survival, there was no significant association between SNA and all-cause survival in four analysis models. Similar results were yielded in the subgroup analyses in terms of PAP and DAP. As for reintervention, in the adjusted analyses of the Cox model, IPTW analysis, and IPTW sensitivity analysis, we found there was no significant association between SNA and reintervention. In patients without PAPs, the subgroup analyses revealed that SNA was associated with a high risk of reintervention: in unadjusted analysis (HR 2.82, 95% CI 1.45–5.51); in the Cox model (HR 2.30, 95% CI 1.13–4.65); and in IPTW sensitivity analysis (HR 3.07, 95% CI 1.40–6.71). IPTW analysis was an exception (HR 2.10, 95% CI 0.89–4.92) [Table 3].

Discussion

We first combined the CFD analyses and clinical cohort analyses in this study, involving 25 idealized models and 722 AAA patients. Hemodynamic results indicated SNA could noticeably increase drag force to influence the stability and safety of implanted stent–grafts. Clinical results suggested that SNA was significantly associated with a higher risk of poor outcomes following EVAR, especially in patients without PAPs or DAPs.

EVAR procedures for SNA patients are generally considered as outside the IFU and have been associated with significant technical difficulties during operation.[4,28,29] The implanted stent–graft is usually held in the proximal attachment zone by friction force, influenced by the radial force of the stent–graft against the proximal neck wall and the contact surface between the stent–graft and the proximal neck wall. SNA patients are more likely to have smaller friction forces. On the one hand, the length of the proximal attachment zone in SNA patients is limited due to the necessary renal artery reservation, leading to a smaller contact surface. On the other hand, the straightening and unsatisfactory morphology of the curved stent–graft further results in a smaller contact surface and a lower radial force. In CFD analyses, we demonstrated that stent–grafts of SNA patients have stronger drag forces. If drag forces exceed friction forces, stent–graft dislocation will become more likely in severely angulated necks.[4] Thus, SNA patients would be advised to receive open surgery, rather than EVAR.

Open surgery is not well tolerated by SNA patients with poor general conditions and high surgical risks. Most AAA patients are generally elderly, and accompanied by serious comorbidities, such as hypertension, diabetes mellitus, COPD, CAD, and stroke.[30] EVAR is considered as the only interventional choice remaining for those patients unsuitable for open surgery. Meanwhile, with the increasing experience of surgeons and the optimization of stent–grafts, EVAR has become the preferred treatment for increasing numbers of SNA patients.[31] According to a recent report, the percentage of SNA patients receiving EVAR has reached up to 29% worldwide.[32]

So far, the influence of SNA on clinical outcomes following EVAR is still controversial. In AbuRahma *et al*'s report,[3] $\beta > 60°$ was associated with a higher early and late-type I endoleak rate. Hobo *et al*[4] summarized the results of 5183 patients in the EUROSTAR registry from 1996 to 2006, showing that SNA was a clear risk factor of T1AEL, proximal neck dilatation, and reintervention. Schanze *et al*,[5] reporting on 10,228 patients between 1999 and 2008 in the United States, also suggested that $\beta > 60°$ was an independent predictor of late sac expansion. Of note, several mixed stent–grafts were applied in the studies cited above, some of which were older generation stent–grafts that were taken off the market many years ago and had low performances in severely angulated necks.

Bastos Goncalves *et al*[15] and Oliveira *et al*[6,16] reported 45 SNA patients and 65 matched nSNA patients from the ENGAGE registry, a large prospective and multicenter cohort of patients using the Endurant stent–graft (Medtronic). The in-hospital, 30-day outcomes revealed no differences regarding early T1AEL, survival, or major complications.[15] Mid-term results (4-year follow-up) also indicated that SNA did not affect T1AEL, neck-related adverse events, and reintervention.[16] However, long-term outcomes (7-year follow-up) identified a higher rate of T1AEL in SNA patients.[6] For other devices specifically designed for compatibility with SNA anatomy, the Aorfix stent–graft (Lombard Medical, Irvine, CA, USA) showed comparable outcomes in graft migration or type I/III endoleak between groups at the 5-year follow-up, but stent–graft fracture occurred in 23% patients at the proximal attachment zone.[7] The Anaconda stent–graft (Vascutek, Inchinnan, Glasgow, United Kingdom) was applied in 36 patients, and the 4-year primary clinical success was 69%, with one migration and seven occlusions.[8] It should be noted that many of these studies were limited by small sample sizes. Thus, recent practice guidelines have no specific recommendations on whether EVAR should be applied in SNA patients,[33,34] and more studies are awaited to verify the influence of SNA on outcomes following EVAR.

Our current study first explored the neck angle change before and after EVAR, and then calculated the postoperative α and β angles according to the linear regression relationships. Next, we constructed 16 SNA and 9 nSNA idealized models for 1 year post-EVAR, to perform CFD analyses. The hemodynamic results indicated that SNA evidently increased drag force, thereby influencing the stability and safety of the implanted stent–grafts. This was further confirmed by clinical results. In the whole cohort, we found that SNA was associated with a significant risk of adverse limb events. However, in patients without PAPs or DAPs, subgroup analyses suggested that SNA was associated with a significant risk of T1AEL and adverse limb events. The above results demonstrated the negative influence of SNA on clinical outcomes after EVAR. Of note, subgroup analyses in patients with PAPs or DAPs showed no significant difference between nSNA and SNA groups in terms of T1AEL, adverse limb event, overall survival, or reintervention, which indicated that appropriate additional procedures in SNA patients could significantly improve the clinical outcomes of EVAR.

For patients undergoing EVARs, good fixation and proper sealing are paramount for long-term clinical success. Appropriate additional procedures can strengthen the stability of stent–grafts by achieving good fixation and proper sealing. Proximal neck dilation with a compliant aortic balloon can eliminate potential channels between the surface of the stent–graft and the aortic wall to improve the contact surface. Implantation of a covered cuff stent can increase the friction force of the stent–graft by exerting a higher radial force, resulting in better adherence.[35,36] Moreover, the Heli-FX aortic system (Aptus Endosystems, Sunnyvale, CA, USA), which is another PAP not applied in this study, mechanically fixes the stent–graft to the aortic neck wall using the Endo Anchor acting as a screw, thus showing high efficacy and durability in the prevention of TIAEL in hostile neck anatomies.[37,38] These PAPs can decrease the risk of stent–graft migration and T1AEL. Similarly, DAPs, including distal neck dilation and the limb extension to the external iliac artery, also strengthen the friction force of the digital stent–graft to lower the risk of T1BEL, T3EL, and limb occlusion. Therefore, for SNA patients, appropriate additional procedures may greatly benefit post-EVAR prognoses.

Several other new techniques, such as the fenestrated endovascular repair and chimney graft technique, have been successfully applied in patients with complex hostile aortic neck anatomies.[39,40] However, their use is not always accessible to most AAA patients due to the procedures' high costs and technical complexity and is therefore limited to high-volume clinical centers with rich experience.

Several limitations deserve consideration. First, the retrospective design may have introduced reporting biases and inherent differences on baseline characteristics. However, all patients were treated consecutively with the same stent–graft by the same team in a single center and during the same time. To further adjust any potential confounding factors, we used the Cox model, IPTW analysis, IPTW sensitivity analysis, and subgroup analysis to explore the influence of SNA on clinical outcomes. Second, stent–graft migration was not analyzed in this study. DUS, recommended by two recent practice guidelines,[33,34] can offer repeated and reliable assessment at low cost without involving exposure to ionizing radiation or nephrotoxic contrast. More patients prefer to receive DUS follow-up. But DUS has no reliable ability to detect stent–graft migration. Meanwhile, the results of the ENGAGE registry using Endurant stent–graft showed an extremely low rate of stent–graft migration (1/1263) at the 5-year follow-up.[41] Third, all idealized models presupposed a homogeneously rigid wall, and the effect of thrombosis between the stent–graft and the aneurysmal aortic wall was not considered in the CFD analysis. Finally, the effect of the cardiac cycle was also not considered in the CFD analysis.

In conclusion, SNA has a critical influence on hemodynamic and clinical outcomes following EVAR for AAA patients. Appropriate additional procedures may be of great benefit to the outcomes of SNA patients. Regular imaging surveillance is necessary for all AAA patients, especially SNA patients. Future comparative studies concerning the influence of SNA are warranted.

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Conflicts of interest

None.

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