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Hidden blood loss in anterior cervical discectomy and fusion with zero-profile anchored spacer for the treatment of cervical radiculopathy

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ABSTRACT

Objectives: This study aims to evaluate the hidden blood loss (HBL) and its possible risk factors after anterior cervical discectomy and fusion (ACDF) with zero-profile anchored spacer (ZPAS) in patients with cervical radiculopathy.

Patients and methods: Between January 2017 and January 2024, a total of 92 patients (44 males, 48 females; mean age: 73.2±10.0 years; range, 44 to 85 years) who underwent ACDF with ZPAS were retrospectively analyzed. Data collection encompassed baseline demographics including age, sex, height, weight, body mass index (BMI), disease duration, symptomatic laterality, and comorbidities and perioperative parameters such as the American Society of Anesthesiologists (ASA) score, operative levels, surgical time, intraoperative blood loss, and postoperative drainage volume. The HBL was quantified using the Sehat formula. Subsequent multivariate linear regression modeling was employed to identify independent predictors of HBL.

Results: The mean surgical time was 152.6±27.6 min. The mean total blood loss (TBL) and HBL were 334.6±67.7 mL and 268.1±69.0 mL, respectively. Correlation analyses revealed significant associations between HBL and symptomatic laterality, hematocrit (Hct) loss, surgical levels, and surgical time (p<0.05). Multivariate linear regression further confirmed Hct loss, surgical levels, and surgical time as positive predictors of HBL (p<0.05).

Conclusion: Patients with cervical radiculopathy who underwent ACDF with ZPAS perioperatively had significant HBL. More Hct loss, more surgical levels, and longer surgical time were independent risk factors for increased HBL.

Keywords: Anterior cervical discectomy and fusion, cervical radiculopathy, hidden blood loss, risk factors, spine surgery.

Anterior cervical discectomy and fusion (ACDF) remains a cornerstone surgical intervention for degenerative cervical pathologies, offering reliable decompression and stabilization outcomes.[1] While traditional ACDF techniques utilizing plate-and-cage constructs have demonstrated efficacy, concerns persist regarding complications such as postoperative dysphagia, esophageal irritation, and adjacent segment degeneration (ASD).[2] The introduction of zero-profile anchored spacers (ZPAS) has revolutionized the field by eliminating anterior plating, thereby reducing soft tissue trauma and theoretically minimizing perioperative morbidity.[1] However, emerging evidence highlights the underrecognized role of hidden blood loss (HBL) in spinal surgeries,[3] which may contribute to hemodynamic instability, delayed recovery, and increased transfusion requirements.[4] Despite its minimally invasive design, ZPAS procedures exhibit clinically significant HBL[5] which remains systematically understudied.

Recent studies have predominantly focused on overt intraoperative blood loss (IBL) in ACDF, while HBL, resulting from hemolysis, extravasation into

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third spaces, or postoperative drainage, remains poorly quantified, particularly in zero-profile procedures.[6] A 2018 retrospective study by Wen et al.[7] underscored that HBL accounted for up to 50% of total blood loss (TBL) in cervical spine surgeries.[7] Furthermore, the biomechanical properties of zero-profile implants, including reduced interspace preparation and minimized endplate disruption, may paradoxically alter bleeding patterns compared to conventional techniques.[8] Current literature also identifies modifiable risk factors such as sex, American Society of Anesthesiologists (ASA) physical status classification, IBL, operation time, multilevel involvement, and patient-specific coagulopathic profiles,[5,7,9] but these have not been systematically evaluated in the context of anchored spacer designs.

Paradoxically, while endoscopic and open ACDF techniques have received attention for HBL quantification,[5,10] the reduced IBL characteristic of ZPAS has inadvertently obscured recognition of its HBL burden. Despite its minimally invasive label,[11] postoperative anemia persists in a subset of cases.[5] This incidence rate substantially exceeds expectations derived from the minimally invasive paradigm traditionally associated with ACDF procedures. To elucidate this discrepancy, in the present study, we aimed to evaluate the HBL and its possible risk factors after ACDF with ZPAS in patients with cervical radiculopathy.

PATIENTS AND METHODS

This single-center, retrospective cohort study was conducted at District People’s Hospital of Chengdu, Department of Department of Orthopaedics between January 2017 and January 2024. Initially, patients undergoing ACDF with ZPAS for cervical radiculopathy were screened. All procedures adhered to contemporary ACDF guidelines and were performed by a senior spinal surgeon. Inclusion criteria were as follows: *(i)* aged ≥18 years; *(ii)* confirmed diagnosis of cervical radiculopathy via clinical and radiographic evaluation; *(iii)* refractory to ≥3 months of structured conservative management with persistent functional impairment; and *(iv)* exclusive use of ZPAS systems. Exclusion criteria were as follows: *(i)* prior cervical spine surgery; *(ii)* cervical pathologies secondary to neoplasms, trauma, or infection; *(iii)* coagulopathies or chronic use of antiplatelet/anticoagulant agents; *(iv)* intraoperative antifibrinolytic administration; and *(v)* incomplete perioperative documentation. Finally, a total of 92 patients (44 males, 48 females; mean age: 73.2±10.0 years; range, 44 to 85 years) who met the inclusion criteria were recruited. Written informed consent was obtained from each patient. This was an observational study. The ethics committee of Pidu District People's Hospital of Chengdu had confir med that no ethical approval is required. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Surgical technique

Following induction of general anesthesia, the patients were positioned supine with cervical spine maintained in neutral alignment and mild extension. A right-sided transverse cervical incision was made, followed by localization of the pathological intervertebral space under intraoperative fluoroscopy. Surgical exposure included sequential distraction of the vertebral space using a Caspar-type retractor, complete resection of the anterior longitudinal ligament and annulus fibrosus, and meticulous discectomy with endplate preparation to the posterior annulus. In case of osteophyte hyperplasia at the posterior edge of the vertebral body, it was removed with a lamina osteoclastic forceps until the dural sac was clearly visible. Distractor tension was calibrated to restore physiological cervical lordosis and intervertebral height. Zero-P implant trials were inserted under direct visualization to achieve optimal footprint coverage confirmed by fluoroscopic verification. Definitive implants were impacted using a dedicated inserter, followed by distractor release and fluoroscopic verification of implant positioning. Bilateral self-tapping screws were placed via a guided targeting system, with screw trajectories monitored in real-time. Hemostasis was confirmed prior to placement of a closed suction drain and layered closure.

Postoperative protocol included: *(i)* cervical orthosis-assisted ambulation on postoperative Day 1, *(ii)* drain removal within 48 h, *(iii)* discharge between postoperative Days 3 to 5, and *(iv)* continued cervical immobilization for three months.

Data collection

Demographic and clinicolaboratory parameters were systematically stratified into two domains:

1. Epidemiological profile: age, sex, height, weight, body mass index (BMI), tobacco use history, pre-existing comorbidities, disease duration, symptomatic laterality.

2. Perioperative metrics: Fasting blood glucose, hematocrit (Hct) levels, serum albumin concentrations, hemoglobin (Hb), ASA physical status classification, surgical levels, surgical time, IBL, and cumulative postoperative drainage.

Notably, no patients received perioperative allogeneic blood transfusions during the study period. These metrics were derived from standard preoperative Day 1 and postoperative Day 2 blood work, including complete blood count and liver function panels.

Calculation of blood loss

The TBL was operationally defined as the composite of HBL and visible blood loss (VBL), with the latter encompassing both IBL and postoperative drainage volume. The HBL was mathematically derived as TBL minus VBL.[12] This necessitated independent quantification of TBL and VBL through validated methodologies.

Total blood loss computation followed the Gross equation:[13] TBL (mL)=(Preoperative blood volume [PBV] [L] × [Hct_{pre}-Hct_{post}]/Hct_{ave}) ×1000

where Hct_{ave} was the average of Hct_{pre} and Hct_{post}.

Preoperative blood volume was calculated using Nadler's gender-specific anthropometric model:[14]

Preoperative blood volume (L)=0.3669h3 + 0.03219w + 0.6041 (male); 0.3561h3 + 0.03308w + 0.1833 (female), with h=height (m) and w=weight (kg). The Hct values were obtained 48 h postoperatively to account for hemodynamic equilibration.[13]

The IBL quantification incorporated gravimetrically measured suction canister contents (corrected for irrigation fluid volume) and Hb mass in surgical gauzes (spectrophotometric analysis). All surgical gauzes were individually processed. Each gauze was rinsed in 500 mL normal saline to elute Hb. The eluent was centrifuged at 3,000 rpm for 10 min, and supernatant Hb concentration measured spectrophotometrically (Cary 60 UV-Vis, Agilent Technologies, CA, USA) at 540 nm wavelength. Calibration curves were generated daily using human Hb standards (0.1-25 g/dL, Sigma-Aldrich H7379). Anemia was classified using WHO sex-specific Hb thresholds (<120 g/L females, <130 g/L males).[15]

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Continuous data were expressed in mean ± standard deviation (SD) or median (min-max), while categorical data were expressed in number and frequency. The analytical framework incorporated parametric correlation assessment (Pearson r for Gaussian-distributed variables) and non-parametric alternatives (Spearman ρ for skewed distributions), complemented by multivariate linear regression modeling to isolate HBL-associated predictors. Model diagnostics included evaluation of residual distributions through the Kolmogorov-Smirnov testing augmented by graphical validation via quantile-quantile plots and kernel density histograms. Variance decomposition analysis was implemented to quantify predictor effect sizes within the final regression architecture. A two-tailed p value of <0.05 was considered statistically significant.

RESULTS

The mean BMI was 22.9±2.2 kg/m². The most prevalent comorbidity was diabetes mellitus (DM). The mean Hb loss and Hct loss were 12.5±5.6 g/L and 3.0±0.7%, respectively. The proportion of patients with anemia increased from 26.1% preoperatively to 77.2% postoperatively. Notably, patients aged ≥75 years (n=41, 44.6%) exhibited greater Hb loss than younger patients (14.3±4.8 g/L *vs.* 10.9±5.7 g/L; p=0.003), despite comparable HBL volumes (271.6±70.1 mL *vs.* 265.2±68.3 mL; p=0.65). The mean surgical time was 152.6±27.6 min. The IBL was 42.5±9.6 mL, while postoperative drainage volume measured 24.0±6.7 mL. The mean HBL and TBL were 268.1±69.0 mL and 334.6±67.7 mL, respectively (Table I).

Correlations between each investigated parameter and HBL were analyzed using the Pearson or Spearman tests (Table II). Symptomatic laterality, Hct loss, surgical levels, and surgical time all showed significant positive correlations with HBL (p<0.05). Subsequent multivariate linear regression analysis identified Hct loss, surgical levels, and surgical time as independent risk factors for increased HBL following ACDF with ZPAS (p<0.05). The HBL increased by 0.359 mL for each 1-min increase in surgical time (Table III).

The post-hoc threshold analysis identified clinically meaningful cut-offs: *(i)* Surgical levels ≥3 increased HBL by >120 mL *vs.* 1-2 levels; *(ii)* Hct loss >3.5% optimally predicted massive HBL (area under the curve [AUC]=0.84); *(iii)* Surgical time >180 min marked a non-linear HBL acceleration point.

TABLE I
Patients' demographics and clinico-laboratory factors

Variables	n	%	Mean±SD
Age (year)			73.2±10.0
Sex			
Male	44	47.8	
Female	48	52.2	
Height (m)			1.66±0.05
Weight (kg)			63.4±7.2
Body mass index (kg/m^2)			22.9±2.2
Tobacco use	22	23.9	
Comorbidities			
Hypertension	11	12.0	
Diabetes mellitus	26	28.3	
Coronary heart disease	11	12.0	
Disease duration (months)			19.1±6.9
Symptomatic laterality			
Unilateral	42	45.7	
Bilateral	50	54.3	
Preoperative blood glucose (mmol/L)			6.1±1.1
Preoperative serum albumin (g/L)			36.5±2.7
Preoperative Hb (g/L)			129.4±6.8
Postoperative Hb (g/L)			116.9±8.7
Hb loss (g/L)			12.5±5.6
Preoperative Hct (%)			37.5±3.0
Postoperative Hct (%)			34.5±2.7
Hct loss (%)			3.0±0.7
ASA classification			
I	7	7.6	
II	63	68.5	
III	22	23.9	
Anemia			
Preoperative anemia	24	26.1	
Postoperative anemia	71	77.2	
Surgical levels			
One	31	33.7	
Two	28	30.4	
Three	33	35.9	
Surgical time (min)			152.6±27.6
Hidden blood loss (mL)			268.1±69.0
Intraoperative blood loss (mL)			42.5±9.6
Postoperative drainage (mL)			24.0±6.7
Total blood loss (mL)			334.6±67.7
Total	92	100	

SD: Standard deviation; Hb: Hemoglobin; Hct: Hematocrit; ASA: American Society of Anesthesiologist.

DISCUSSION

Anterior cervical discectomy and fusion remains a gold-standard surgical approach for cervical degenerative disease. The integration of ACDF with ZPAS has demonstrated advantages including reduced intraoperative trauma, lower rates of dysphagia, and decreased incidence of ASD compared to conventional techniques.[16] Owing to its

TABLE II
Correlation analysis between related factors and HBL

Variables	*p*	Correlation
Age	0.676	0.044
Sex	0.305	-0.108
Height	0.462	0.078
Weight	0948	0.007
Body mass index	0.750	-0.034
Tobacco use	0.116	-0.165
Comorbidities	0.633	-0.051
Disease duration	0.386	-0.092
Symptomatic laterality	<0.001	0.700
Preoperative blood glucose	0.321	0.105
Preoperative serum albumin	0.868	-0.018
Preoperative Hb	0.248	-0.122
Postoperative Hb	0.555	-0.062
Hb loss	0.772	0.031
Preoperative Hct	0.085	0.180
Postoperative Hct	0.907	-0.102
Hct loss	<0.001	0.789
ASA classification	0.076	0.186
Preoperative anemia	0.846	0.021
Postoperative anemia	0.193	0.137
Surgical levels	<0.001	0.926
Surgical time	<0.001	0.777
Intraoperative blood loss	0.170	-0.144
Postoperative drainage	0.631	-0.051
Total blood loss	0.682	-0.043

HBL: Hidden blood loss; Hb: Hemoglobin; Hct: Hematocrit; ASA: American Society of Anesthesiologists.

superior clinical outcomes, ZPAS has progressively supplanted traditional plate-cage constructs as the primary implant for single- and two-level ACDF procedures. A growing body of evidence supports the efficacy of ZPAS-augmented ACDF even in multilevel interventions, as highlighted in recent studies.[2,17] Despite its minimally invasive advantages, ACDF is still associated with a clinically significant incidence of postoperative anemia in practice. In our cohort, a marked decline in Hb level was observed postoperatively (mean reduction: 12.5±5.6 g/L), with the majority of patients being elderly. Our data reveal a paradoxical dissociation: while HBL magnitude was age-independent (r=0.044, p=0.676), older patients (≥75 years) experienced significantly greater Hb loss. We propose three mechanistic explanations: reduced hematopoietic reserve, hemodilution vulnerability and comorbidity synergism. These findings underscore the necessity of optimizing perioperative blood management to mitigate hemorrhage-related complications and enhance recovery, a priority for this geriatric population. Notably, TBL in our study exceeded the sum of IBL and postoperative drainage volume, indicating substantial unaccounted blood loss (i.e., HBL). The mean HBL reached 268.1±69.0 mL. Significant HBL may lead to prolonged hospitalization and postoperative anemia. These complications are associated with impaired organ perfusion, increased risk of cerebrovascular events, and heightened susceptibility to surgical site infections.[18,19]

Previous studies have proposed mechanisms for HBL, such as tissue blood extravasation and hemolytic processes.[20] Unlike these mechanistic studies, the present investigation focuses on identifying clinical risk factors for HBL. Using multivariate linear regression, we determined key predictors associated with increased HBL. Our findings indicated that greater HBL correlated with more Hct loss, increased surgical levels, and extended surgical time.

In the present study, there was a significant positive correlation between Hct loss and HBL (β=0.226, p<0.001). A reduction in Hct may reflect intraoperative fluid shifts or postoperative hemodilution, contributing to an increase in the

TABLE III
Multiple linear regression analysis of influencing factors on HBL following ACDF

Independent variables	B value	SE	β	t	*p*
Constant	37.403	18.168	-	2.059	0.043
Symptomatic laterality	12.435	7.549	0.090	1.647	0.103
Hct loss	21.123	5.687	0.226	3.714	<0.001
Surgical levels	46.592	6.113	0.566	7.622	<0.001
Surgical time	0.359	0.159	0.144	2.262	0.026

HBL: Hidden blood loss; ACDF: Anterior cervical discectomy and fusion; SE: Standard error; Hct: Hematocrit; R^2=0.863, adjusted R^2=0.857, F=136.897, p=0.000.

observed HBL.[21] Zhou et al.[22] reported that a 1% decrease in Hct corresponded to an average increase of 39.861 mL in HBL.[22] Clinically, preoperative anemia correction (e.g., iron supplementation or erythropoietin) and intraoperative Hct monitoring are critical to mitigating HBL risk. Additionally, restricting excessive postoperative fluid administration may help minimize hemodilution-related Hct decline.

The number of surgical levels was the strongest predictor of HBL (β=0.566, p<0.001), with each additional level increasing HBL by 46.592 mL. Multilevel procedures necessitate extensive soft tissue dissection and prolonged bone exposure, exacerbating capillary leakage and interstitial fluid loss. A descriptive study found that HBL was significantly correlated with multi-segment fusion.[23] To address this, minimally invasive techniques and topical hemostatic agents are recommended to reduce tissue trauma and intraoperative bleeding.[24,25]

Prolonged surgical time was weakly, but significantly associated with HBL (β=0.144, p=0.026). Cai et al.[5] found that for every additional minute of ACDF surgery, HBL increased by 2.179 mL. Potential mechanisms include *(i)* ischemia-reperfusion injury from prolonged tissue retraction, *(ii)* prolonged exposure of surgical surfaces, and *(iii)* anesthetic-induced coagulopathy. Strategies to reduce surgical time include preoperative imaging-based planning, enhanced surgical team coordination, and advanced instrumentation (e.g., ultrasonic bone curettes).

Nonetheless, this study has several limitations. First, the retrospective design from a single institution and limited cohort size may reduce the statistical power of parameter estimates. Second, reliance on Hct measurements obtained as late as postoperative Day 2 for HBL quantification may still risk inaccuracies. While very early measurement (e.g., postoperative Day 0) could underestimate loss due to unreplaced volume, delayed assessment on postoperative Day 2 may miss the peak hemodilution effect from intraoperative fluid administration. By this time, ongoing fluid shifts, blood loss into tissues, or early mobilization may have altered hemodynamics, potentially obscuring the true nadir of Hct relevant to HBL calculation. Additionally, postoperative fluid resuscitation could dilute hematological parameters, introducing potential measurement bias in HBL calculations. To address these constraints, future multi-center prospective studies with expanded cohorts and serial Hct monitoring protocols are warranted to validate these findings and refine HBL assessment methodologies. There was no follow-up and no mention of patients' outcomes (e.g., complications, delayed recovery, infections) associated with HBL.

In conclusion, HBL tends to be underestimated in patients with cervical radiculopathy undergoing ACDF with ZPAS, particularly among those with greater Hct loss, multilevel procedures, or prolonged surgical time. Consequently, spine surgeons should prioritize recognizing these risk factors for HBL and optimize perioperative management strategies to mitigate its adverse clinical impacts.

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