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Structural Heart
The Journal of the Heart Team

ISSN: 2474-8706 (Print) 2474-8714 (Online) Journal homepage: https://www.tandfonline.com/loi/ushj20

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To cite this article: Nay M. Htun, Gidon Y. Perlman, Danny Dvir, Adrian Attinger-Toller, Giuseppe Martucci, David Wood, Nicolo Piazza & John G. Webb (2017) A Novel Valvuloplasty Scoring Balloon Catheter for Aortic Stenosis, Structural Heart, 1:5-6, 285-290, DOI: 10.1080/24748706.2017.1378459

To link to this article: https://doi.org/10.1080/24748706.2017.1378459

Accepted author version posted online: 12 Sep 2017.
Published online: 26 Sep 2017.

STRUCTURAL HEART
2017, VOL. 1, NOS. 5–6, 285–290
https://doi.org/10.1080/24748706.2017.1378459

ORIGINAL RESEARCH

A Novel Valvuloplasty Scoring Balloon Catheter for Aortic Stenosis

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ABSTRACT

Background: There has been a renewed interest in balloon aortic valvuloplasty (BAV) since the inception of transcatheter aortic valve replacement (TAVR) in treating aortic stenosis (AS). This study aimed to demonstrate the safety and feasibility of a novel aortic valvuloplasty balloon catheter for the treatment of symptomatic severe aortic valve stenosis.

Methods: Data from 25 patients who underwent BAV with the AngioSculpt Valvuloplasty Scoring Balloon Catheter at two Canadian centers with clinical follow-up and echocardiographic assessment at 30 days, 6 months, and 12 months were analyzed.

Results: Mean age of the patients was 83.6 ± 5.8 years with 68% females. Mean gradient across the aortic valve was 44.0 ± 15.1 mmHg pre- and 33.6 ± 13.8 mmHg post-valvuloplasty (average reduction of 24% post-BAV, $p < 0.05$). 38% of patients showed ≥ 30% aortic gradient reduction. There were no major adverse cardiovascular events. Stroke and major vascular complication rates were zero. Two patients had moderate aortic regurgitation post-valvuloplasty.

Conclusion: Preliminary results with a novel valvuloplasty scoring balloon for aortic stenosis demonstrate no safety concerns with a favorable gradient reduction. Additional studies will be required to demonstrate clinical utility in selected patients.

ARTICLE HISTORY Received 23 May 2017; Accepted 6 September 2017

KEYWORDS Aortic stenosis; balloon aortic valvuloplasty; AngioSculpt novel valvuloplasty scoring balloon; transcatheter aortic valve replacement; valvular heart disease

Introduction

With the emergence of transcatheter aortic valve replacement (TAVR) as a viable alternative to surgical aortic valve replacement, there is a renewed interest in balloon aortic valvuloplasty (BAV).

BAV for calcific aortic stenosis (AS) was first described by Cribier and colleagues in 1986.[1] Despite initial enthusiasm, BAV traditionally has only a limited role in the management of aortic stenosis due to its high recurrence rate without a significant mortality benefit.[2] BAV has been used either as a stand-alone therapy for alleviation of symptoms, as a bridge to a more definitive therapy, and in this era of TAVR, for pre- or post-dilation of transcatheter heart valves (THV), annular sizing, evaluating the risk of coronary occlusion, or as a diagnostic procedure in complex cases where the significance of AS is not entirely clear.

The complications related to BAV are not trivial with an in-hospital mortality rate of up to 2–2.5%, stroke rate of 0.9–2.3%, and major vascular complication rate up to 8.6% in some recent reports.[3–6] Hence the need for more refined devices for BAV seems logical especially as BAV has been used more frequently for broader indications.

In this study, we aimed to investigate the safety and feasibility of a novel AngioSculpt Valvuloplasty Scoring Balloon Catheter for the treatment of severe aortic valve stenosis.

Materials and methods

Study population

The study was a non-randomized single-arm prospective first-in-human study in two major tertiary centers in Canada (St Paul's Hospital, Vancouver, British Columbia and McGill University Hospital, Montreal, Quebec). The AngioSculpt Valvuloplasty Scoring Balloon Catheter was used as a stand-alone treatment or "bridge" to TAVR. The study was approved by local Institutional Review Board/Ethics Committee at both sites. A total of 25 patients with symptomatic, degenerative, tricuspid, severe aortic valve stenosis, who were not surgical candidates, were consecutively recruited between June 2012 and September 2014. All participants signed the ethics committee approved informed consent form. The inclusion and exclusion criteria for the study are shown in Table 1.

Angiosculpt Valvuloplasty Scoring Balloon Catheter

The AngioSculpt Valvuloplasty Scoring Balloon Catheter (Spectranetics Corporation, CO, USA) comprises a

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Supplemental data for this article can be accessed on the publisher's website.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria
(Patients must meet all of the following criteria)
1. Native, degenerative/calcific, tricuspid, aortic stenosis with echocardiographically derived criteria: mean gradient of > 40 mm Hg or Doppler peak systolic velocity greater than 4.0 m/s or an initial aortic valve area < 1.0 cm^2
2. Symptomatic aortic valve disease as demonstrated by NYHA dyspnea Class II or greater
3. Aortic valve annulus diameter ≥ 18 mm and ≤ 28 mm measured on pre-procedure transthoracic echocardiogram (TTE)
4. Not a suitable candidate for elective surgical aortic valve replacement
5. Agrees to return for all required post-procedure follow-up visits
Exclusion criteria
(Patients were excluded from the study if they met one or more of the following criteria)
1. Known hypersensitivity or contraindication to aspirin, heparin, nitinol, nickel or sensitivity to contrast media which cannot be adequately pre-medicated
2. Any sepsis, including active endocarditis
3. Recent myocardial infarction (< 30 days)
4. Unicuspid or bicuspid aortic valve or non-calcific aortic stenosis
5. Concomitant ≥ 2+ aortic regurgitation (AR)
6. Any left ventricular thrombus or mass diagnosed by echocardiography
7. Hypertrophic cardiomyopathy with or without obstruction
8. Severe left ventricular dysfunction with left ventricular ejection fraction (LVEF) < 20%
9. Uncontrolled atrial fibrillation (heart rate greater than 110 bpm)
10. Previous aortic valve replacement (bioprosthetic or mechanical)
11. Cerebrovascular accident (CVA) or transient ischemic attack (TIA) within the previous 6 months
12. Inadequate ilio-femoral arteries (due to size, disease, tortuosity or calcification) to accommodate a standard 12Fr introducer sheath
13. Untreated anemia (hemoglobin <9 g/dL) or thrombocytopenia (platelet count <100,000)
14. Coagulopathy including an international normalized ratio (INR) >2.0
15. Active peptic ulcer, gastrointestinal, or other significant bleeding within the previous 3 months
16. Life expectancy less than 1 year due to co-morbidities
17. Estimated glomerular filtration rate (eGFR) < 30 ml/min in patients not on dialysis
18. Women who are pregnant
19. Patients enrolled in another investigational study

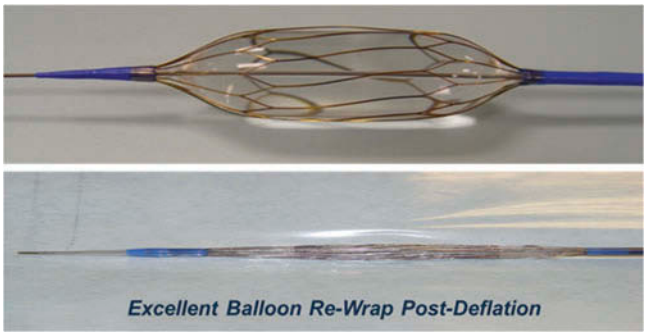

Figure 1. AngioSculpt Valvuloplasty Scoring Balloon Catheter. Upper image: Full inflation of the balloon showing laser cut nitinol scoring element with 4 rings and 12 rectangular struts and atraumatic soft tip. Lower image: Excellent rewrap of the balloon on deflation.

conventional balloon catheter with a unique scoring balloon design. The scoring balloon is semi-compliant with an attached nitinol spiral cage (scoring element). The laser cut nitinol scoring element has 12 spiral struts and four cross-linking stabilizing rings that wrap around the balloon (Figure 1). These struts create focal amplification of the forces exerted by the valvuloplasty balloon along the edges of the scoring element (up to 20 times). Four different sizes of the AngioSculpt Valvuloplasty Scoring Balloon Catheter were available with 18, 20, 22, 24 mm diameter × 4.0 cm length balloons. The design of the system is intended to minimize balloon slippage during inflation and facilitate a more optimal valvuloplasty result with an improved aortic valve area, and a more durable outcome, compared to conventional BAV catheters.

The AngioSculpt Valvuloplasty Scoring Balloon Catheter has been subjected to mechanical tests, biomaterial evaluations, and functional testing in live porcine and sheep models. Phase I study in humans with intra-operative evaluation (Figure 2) immediately prior to surgical aortic valve replacement showed no safety concerns.

Valvuloplasty procedure and follow-up

Patients were pre-treated with acetylsalicylic acid and heparin to maintain an activated clotting time (ACT) of 200–250 seconds. The valvuloplasty procedure was performed using a traditional retrograde femoral artery approach. Right and left heart cardiac catheterization before BAV was carried out to record baseline hemodynamic measurements and calculate the cardiac output as well as aortic valve area. The specific size of the balloon was selected so as to approximate (but not exceed) the estimated aortic valve annular diameter as measured by transesophageal echocardiography or computed tomography angiography. The volume needed to achieve the nominal and rated balloon burst pressures for different sizes of the device are shown in Supplemental Table 1 (online only). BAV was done while ventricular pacing at a rate of approximately 180 bpm (Figure 3). A dual-lumen pigtail catheter was subsequently used to measure the transaortic valve gradient and calculate the aortic valve area. Clinical and echocardiographic follow up was obtained at 30 days, 6 months and 12 months.

Study endpoints

The primary efficacy endpoint was procedural success, defined as a > 50% increase in the aortic valve effective orifice area or a ≥ 30% decrease in the mean aortic valve gradient and ≤ 2+ valvular regurgitation post-BAV as assessed by echocardiography or hemodynamic measurements and angiography. The primary safety endpoint was composite of freedom from in-hospital death, stroke, myocardial infarction (MI) or emergency cardiac surgery.

Secondary endpoints were New York Heart Association (NYHA) functional class of the patients as well as echocardiographic parameters of the aortic valve and left ventricular (LV) function at 30 days, 6 months, and 12 months.

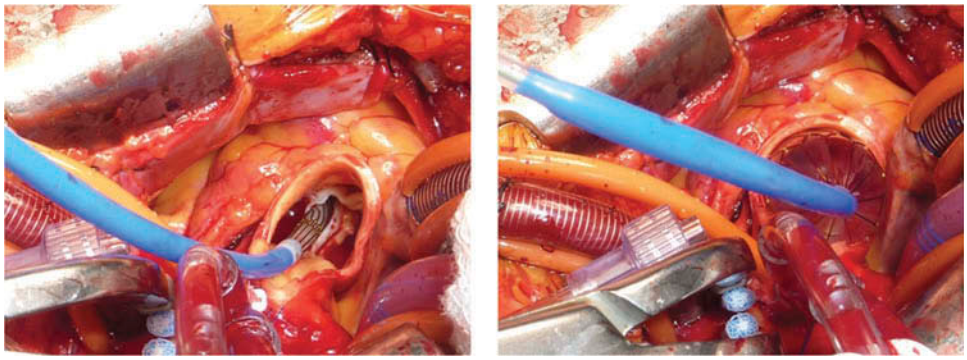

Figure 2. Intra-operative evaluation of AngioSculpt Valvuloplasty Scoring Balloon Catheter. Left: Deflated AngioSculpt balloon across the stenotic native aortic valve. Right: Inflated AngioSculpt balloon deployed across the stenotic aortic valve.

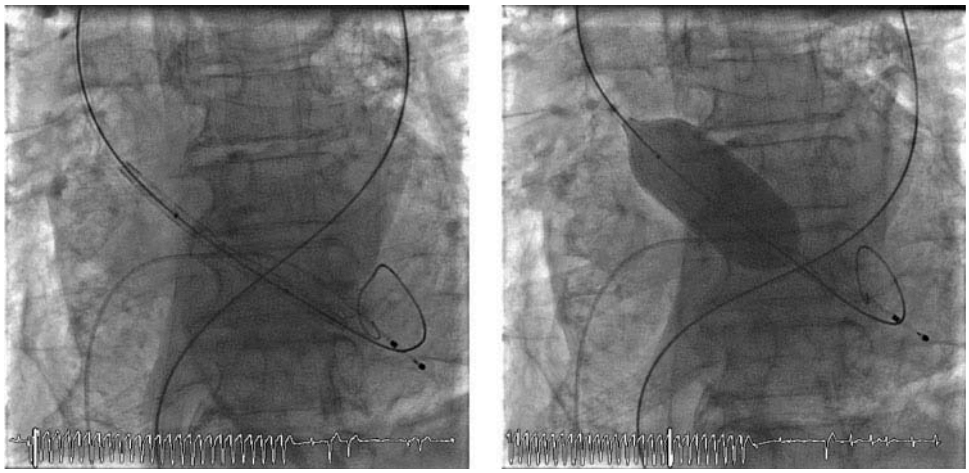

Figure 3. Fluoroscopic images of balloon aortic valvuloplasty (BAV) using AngioSculpt Valvuloplasty Scoring Balloon Catheter. Left: Balloon catheter crossing the native aortic valve. Right: Fully inflated AngioSculpt balloon across the native aortic valve.

Statistics

The data was presented as mean and standard deviation (SD) for continuous variables and as frequency and percentages for categorical variables. Comparison of continuous variables was done using the *t*-test and a *p* value of <0.05 was considered statistically significant. GraphPad Prism 6 software (GraphPad Software, Inc., CA, USA) was used for statistical analysis.

Results

Baseline characteristics

The average age in this cohort was 84 and 68% were female. The primary presenting symptomology was dyspnea in 96% of patients with 88% in NYHA class III or IV. Baseline characteristics are shown in Table 2.

Hemodynamics

The mean aortic gradient decreased from an average of 44 ± 15.1 mmHg pre-BAV to 33.6 ± 13.8 mmHg post-procedure (average of 10.4 mmHg reduction) ($p < 0.05$) (Figure 4) and the aortic valve area increased an average of 0.1 cm^2 ($p < 0.05$). Pre- and post-procedure hemodynamics are given in Table 3.

Follow-up

The majority of patients (19 out of 25) exited the study prior to 12 months (16 exited before 6 months). A total of 15 out of the 19 patients exiting the study had TAVR. Two patients withdrew consent while two patients died of non-cardiac causes (see below).

Primary endpoints

Nine cases achieved the predefined criteria for procedural success (primary efficacy endpoint) in this study (total procedural success rate of 36%) while the primary efficacy endpoint was not met in 64%. The primary safety (a composite of freedom from in-hospital death, stroke, myocardial infarction, or emergency cardiac surgery) was met by all 25 patients.

Table 2. Baseline characteristics.

Baseline characteristics (N = 25)	% or mean ± SD
Age	83.6 ± 5.8
Gender	
Male	32.0%
Female	68.0%
BMI (kg/m^2)	25.3 ± 5.6
Clinical history	
Diabetes	32.0%
Smoking history	60.0%
Hyperlipidemia	76.0%
Hypertension	88.0%
Prior BAV	0
Prior PTCA	24.0%
Prior CABG	8.0%
Prior MI	20.0%
Prior CVA/TIA	24.0%
CHF	64.0%
PVD	20.0%
Renal insufficiency	40.0%
Known significant CAD at time of procedure	80.0%
Single vessel disease	21.1%
Two vessel disease	10.5%
Three vessel disease	68.4%
Indication for aortic valvuloplasty	
High risk	68.0%
Frailty	32.0%
Primary symptomatology	
Dyspnea	95.8%
Angina	4.2%
NYHA Class	
0 or I	0%
II	12.0%
III	64.0%
IV	24.0%

Note. BMI, body mass index; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft; MI, myocardial infarction; CHF, congestive heart failure; PVD, peripheral vascular disease; CAD, coronary artery disease.

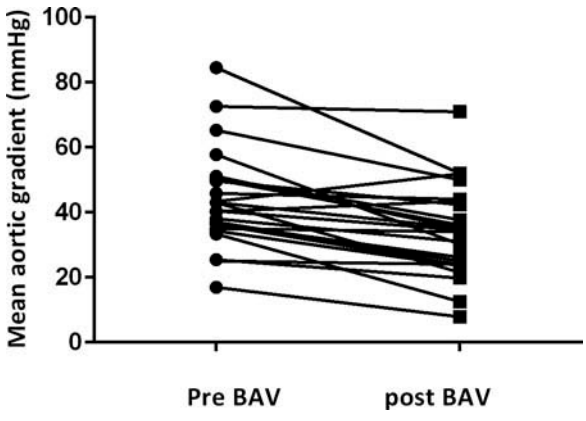

Figure 4. Changes in mean aortic gradient pre and post balloon aortic valvuloplasty (BAV) measured invasively during the procedure. The mean aortic gradient decreased from 44 mmHg pre-BAV to 33.6 mmHg post-BAV (average of 10.4 mmHg reduction) ($p < 0.05$).

Secondary endpoints

NYHA functional class

The NYHA functional class remained similar in patients pre- and immediately post-BAV (88% vs 77% NYHA class III and IV). Some patients showed improvement between discharge and 30 days (77% vs 50% NYHA class III and IV). After 30 days, it was not possible to draw a meaningful conclusion on the change in functional class due to the small sample size and a high rate of early study exit. NYHA class pre- and post-BAV as well as during follow-up is shown in Supplemental Table 2 (online only).

Echocardiographic assessment of aortic valve and left ventricular function

The mean aortic valve gradient measured by echocardiography decreased from a mean of 49.6 mmHg pre-BAV to a mean of 35.1 mmHg post-procedure ($p < 0.05$) associated with an average increase in aortic valve area of 0.2 cm^2 ($p < 0.05$). The mean gradient increased slightly between discharge (35.1 mmHg) and 30 days (39.5 mmHg), but remained reduced compared to pre-procedure values. The percentage of patients with absent or trace AR increased from 17% pre-procedure to 29% post-procedure and 37% at 30 days, largely due to a shift from mild to none/trace. The mean left ventricular ejection fraction (LVEF) remained in the 50–60% range between pre-and 30 days post-procedure. Again it was difficult to draw conclusions form the echocardiographic parameters at 6 and 12 months due to the large number of patients exiting the study. The change in echocardiographic parameters is shown in Table 4.

Adverse events

There were two instances of intra-procedure adverse events. One patient had left iliac artery dissection and was treated conservatively. Another patient had asystole during inflation of the study device requiring chest compression and temporary pacemaker insertion followed by permanent pacemaker implantation. There were two deaths during the follow-up period. One patient died due to intestinal obstruction 30 days post-procedure. A second patient committed suicide prior to 6 month follow-up. One patient experienced myocardial infarction prior to 30 days follow-up, necessitating intervention to the left main coronary artery which had pre-existing significant lesion prior to study enrollment. A summary of adverse events is shown in Table 5.

Discussion

The purpose of this first-in-human study was to demonstrate the safety and feasibility of a novel valvuloplasty device for the treatment of severe aortic valve stenosis.

While the primary efficacy endpoint was only met in 36% of participants, the device achieved an average of 10.4 mm Hg (24%) reduction in mean aortic valve gradient. Overall, 8.3% of patients had moderate aortic regurgitation (AR) post BAV and none had severe AR. The primary safety endpoint of freedom from in-hospital death, stroke, MI or emergency

Table 3. Pre- and post-procedure hemodynamics.

Parameter	Pre-BAV Mean ± SD (*n*)	Post-BAV Mean ± SD (*n*)	Difference Mean ± SD (*n*)
Mean aortic gradient (mmHg)	44.0 ± 15.1 (24)	33.6 ± 13.8 (25)	−10.4 ± 9.3 (24) ($p < 0.05$)
Aortic valve area (cm^2)	0.7 ± 0.4 (22)	0.8 ± 0.4 (25)	0.1 ± 0.2 (22) ($p < 0.05$)
PA pressures (mmHg)			
Systolic	39.8 ± 15.3 (24)	38.4 ± 16.8 (23)	0.4 ± 8.4 (21) (p = ns)
Diastolic	15.4 ± 7.3 (24)	15.0 ± 7.4 (23)	0.1 ± 5.3 (22) (p = ns)
Mean	24.9 ± 11.1 (24)	24.2 ± 10.9 (23)	0.2 ± 6.5 (22) (p = ns)
Pulmonary capillary wedge pressure (mmHg)	14.4 ± 6.4 (20)	15.0 ± 6.0 (17)	0.8 ± 3.7 (16) (p = ns)
Left ventricular end diastolic pressure (mmHg)	17.4 ± 7.3 (15)	17.2 ± 5.4 (12)	−1.8 ± 8.8 (11) (p = ns)
Cardiac output (L/min)	3.7 ± 1.6 (25)	3.5 ± 1.2 (23)	−0.3 ± 0.9 (23) (p = ns)

Note. ns, non-significant; BAV, balloon aortic valvuloplasty; SD, standard deviation; PA, pulmonary artery.

Table 4. Change in echocardiographic parameters.

	Echocardiographic parameters pre-BAV and post-BAV Mean ± SD (*n*) or #/# (%)				
Echocardiographic parameter	Pre-BAV	Post-BAV (pre-discharge)	30 days	6 months	12 months
Mean aortic valve gradient (mmHg)	49.6 ± 20.3 (25)	35.1 ± 10.9 (24)	39.5 ± 10.8 (17)	37.9 ± 13.1 (7)	38.4 ± 14.1 (4)
Aortic valve area (cm^2)	0.6 ± 0.2 (25)	0.8 ± 0.2 (22)	0.8 ± 0.2 (16)	0.8 ± 0.2 (6)	0.6 ± 0.2 (4)
Aortic regurgitation					
None/trace	4/24 (16.7%)	7/24 (29.2%)	7/19 (36.8%)	2/8 (25.0%)	1/4 (25.0%)
Mild	19/24 (79.2%)	15/24 (62.5%)	12/19 (63.2%)	6/8 (75.0%)	3/4 (75.0%)
Moderate	1/24 (4.2%)	2/24 (8.3%)	0/19 (0.0%)	0/8 (0.0%)	0/4 (0.0%)
Severe	0/24 (0.0%)	0/24 (0.0%)	0/19 (0.0%)	0/8 (0.0%)	0/4 (0.0%)
LVEF (%)	54.8 ± 17.6 (24)	56.3 ± 14.0 (19)	57.9 ± 15.2 (14)	46.8 ± 17.0 (5)	40.9 ± 18.5 (4)

Note. BAV, balloon aortic valvuloplasty; SD, standard deviation; LVEF, left ventricular ejection fraction.

Table 5. Adverse events (*n* (%)).

Event	All	Study device or procedure related
Death	2 (8)	0 (0)
MI	1 (4)	0 (0)
Stroke	0 (0)	0 (0)
Vascular complications		
Major	0 (0)	0 (0)
Minor	1 (4)	1 (4)
Pacemaker	1 (4)	1 (4)

Note. MI, myocardial infarction.

cardiac surgery was met in all participants. In the study by Ben-Dor and colleagues[7] which reported the outcomes of 262 patients undergoing traditional BAV procedures, serious adverse events were not insignificant with 1.6% intraprocedural death, 6.9% vascular complications requiring intervention and 1.99% stroke rate. Eltchaninoff and co-authors also reported 2.5% death, 1.5% major vascular complication and 1.8% stroke in their cohort involving 323 patients.[3] No major safety events directly related to the AngioSculpt Valvuloplasty Scoring Balloon Catheter or the procedure were seen in our study.

Limitations of our study were the small number of participants as well as a high proportion of patients leaving the study before the final follow-up of 12 months. Despite a small sample size, this study offers some data highlighting the safety and feasibility of this novel AngioSculpt Valvuloplasty Scoring Balloon Catheter, warranting further evaluation.

Conclusion

The results of this first-in-man study with AngioSculpt Valvuloplasty Scoring Balloon Catheter for symptomatic

severe aortic stenosis appeared to show no safety concerns with a favorable gradient reduction across the aortic valve. Additional studies will be required to demonstrate clinical utility in selected patients in the future.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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