

• 论著 •

二尖瓣反流面积分级对重度主动脉瓣狭窄合并二尖瓣关闭不全患者经导管主动脉瓣置换术后预后的影响



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贺宇^{1, 2}, 牛毅菲², 黄琼³, 林振乾³, 刘荣³, 袁义强^{1, 2}

【摘要】目的 探讨二尖瓣反流面积(MRA)分级对重度主动脉瓣狭窄(AS)合并二尖瓣关闭不全(MR)患者经导管主动脉瓣置换术(TAVR)后预后的影响。**方法** 选取2018年4月至2021年7月在郑州市第七人民医院、河南省胸科医院应用自膨式瓣膜行TAVR的重度AS合并MR患者156例。查阅医院电子病历系统并收集患者的临床资料,所有患者术后1、6、12个月进行门诊或电话随访,记录其主要不良心脑血管事件(MACCE)发生情况。比较患者手术前后超声心动图检查结果,有无MACCE患者性别、年龄、BMI、纽约心脏病协会(NYHA)分级、合并症发生情况、既往手术史及术后超声心动图检查结果。重度AS合并MR患者TAVR后发生MACCE的影响因素分析采用多元Cox回归分析;绘制ROC曲线以评估术后MRA分级对重度AS合并MR患者TAVR后发生MACCE的预测价值。**结果** 156例患者均经股动脉路径TAVR,其中6例患者术中或术后24 h内死亡,最终纳入150例患者。术后患者升主动脉内径、左心室舒张末期内径(LVEDD)、左心室收缩末期内径(LVESD)、室间隔厚度(IVST)、左心房内径(LAD)、MRA小于术前,左心室射血分数(LVEF)高于术前,主动脉瓣最大流速(Vmax)慢于术前,主动脉瓣峰值跨瓣压差(Peak-AVG)低于术前,MRA分级优于术前($P<0.05$)。随访12个月,共32例患者发生MACCE。有无MACCE患者年龄、BMI、NYHA分级为Ⅲ~Ⅳ级者占比、高血压发生率、糖尿病发生率、心房颤动发生率及术后LVEF、LVEDD、LVESD、IVST、LAD、MRA分级>2级者占比比较,差异有统计学意义($P<0.05$)。多元Cox回归分析结果显示,术后LVEF[HR=0.927, 95%CI(0.888, 0.968)]、IVST[HR=0.505, 95%CI(0.362, 0.703)]、LAD[HR=1.185, 95%CI(1.072, 1.309)]、MRA分级[HR=3.336, 95%CI(1.119, 9.946)]是重度AS合并MR患者TAVR后发生MACCE的独立影响因素。ROC曲线分析结果显示,术后MRA分级预测重度AS合并MR患者TAVR后发生MACCE的曲线下面积为0.869[95%CI(0.802, 0.935), $P<0.001$]。**结论** TAVR可有效改善重度AS合并MR患者的心功能及减轻其二尖瓣反流程度,术后MRA分级升高是重度AS合并MR患者TAVR后发生MACCE的危险因素,且其对患者TAVR后发生MACCE有较好的预测价值。

【关键词】 主动脉瓣狭窄;二尖瓣关闭不全;二尖瓣反流;经导管主动脉瓣置换术;预后

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Effect of Mitral Regurgitation Area Grading on Prognosis after Transcatheter Aortic Valve Replacement in Patients with Severe Aortic Valve Stenosis Combined with Mitral Valve Regurgitation HE Yu^{1,2}, NIU Yifei², HUANG Qiong³, LIN Zhenqian³, LIU Rong³, YUAN Yiqiang^{1,2}

1.The Second School of Clinical Medical University, Southern Medical University, Guangzhou 510515, China

2.Cardiovascular Internal Medicine, the 7th People's Hospital of Zhengzhou, Zhengzhou 450006, China

3.Cardiovascular Internal Medicine, Henan Provincial Chest Hospital, Zhengzhou 450008, China

Corresponding author: YUAN Yiqiang, E-mail: zzqyyuanyiqiang@126.com

【Abstract】 Objective To investigate the effect of mitral regurgitation area (MRA) grading on prognosis after transcatheter aortic valve replacement (TAVR) in patients with severe aortic stenosis (AS) combined with mitral valve regurgitation (MR). **Methods** A total of 156 patients with severe AS combined with MR who underwent TAVR with self-expandable valves in the 7th People's Hospital of Zhengzhou and Henan Provincial Chest Hospital from April 2018 to July 2021 were selected. The electronic medical record system of the hospital was consulted and the clinical data of the patients were collected. All patients

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1.510515广东省广州市,南方医科大学第二临床医学院 2.450006河南省郑州市第七人民医院心血管内科 3.450008河南省郑州市,河南省胸科医院心血管内科

通信作者: 袁义强, E-mail: zzqyyuanyiqiang@126.com

were followed up by outpatient or telephone at 1, 6 and 12 months after operation, and the occurrence of major adverse cardiac and cerebrovascular events (MACCE) was recorded. The echocardiography results of patients before and after surgery were compared. Gender, age, BMI, New York Heart Association (NYHA) grading, comorbidities, previous surgical history and postoperative echocardiography results of patients with or without MACCE were compared. Multivariate Cox regression analysis was used to analyze the influencing factors of MACCE after TAVR in patients with severe AS combined with MR. The ROC curve was drawn to evaluate the predictive value of postoperative MRA grading for MACCE after TAVR in patients with severe AS combined with MR.

Results All 156 patients underwent TAVR via femoral artery. Six patients died during operation or within 24 h after operation. Finally, 150 patients were included. After operation, the internal diameter of ascending aorta, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), interventricular septum thickness (IVST), left atrial diameter (LAD) and MRA were smaller than those before operation, left ventricular ejection fraction (LVEF) was higher than that before operation, the maximum velocity on aortic valve (Vmax) was slower than that before operation, the peak-aortic valve gradient (Peak-AVG) was lower than that before operation, and MRA grading was better than that before operation ($P < 0.05$). During the 12-month follow-up, MACCE occurred in 32 patients. There were significant differences in age, BMI, proportion of NYHA grading of III–IV, incidence of hypertension, incidence of diabetes, incidence of atrial fibrillation and postoperative LVEF, LVEDD, LVESD, IVST, LAD, proportion of MRA grading ≥ 2 in patients with or without MACCE ($P < 0.05$). Multivariate Cox regression analysis showed that postoperative LVEF [$HR=0.927$, 95%CI (0.888, 0.968)], IVST [$HR=0.505$, 95%CI (0.362, 0.703)], LAD [$HR=1.185$, 95%CI (1.072, 1.309)] and MRA grading [$HR=3.336$, 95%CI (1.119, 9.946)] were independent influencing factors of MACCE after TAVR in patients with severe AS combined with MR. ROC curve analysis showed that the area under the curve of postoperative MRA grading in predicting MACCE after TAVR in patients with severe AS combined with MR was 0.869 [95%CI (0.802, 0.935)], $P < 0.001$. **Conclusion** TAVR can effectively improve the cardiac function of patients with severe AS combined with MR and reduce their degree of mitral regurgitation. Elevated postoperative MRA grading is a risk factor for MACCE after TAVR in patients with severe AS combined with MR, and it has a better predictive value for MACCE after TAVR in patients.

[Key words] Aortic valve stenosis; Mitral valve regurgitation; Mitral regurgitation; Transcatheter aortic valve replacement; Prognosis

主动脉瓣狭窄（aortic valve stenosis，AS）是常见的心脏瓣膜病，近年来随着人口老龄化进程加剧，其患病率逐年升高。目前，经导管主动脉瓣置换术（transcatheter aortic valve replacement，TAVR）是重度AS患者的一线治疗方法^[1]。但由于行TAVR的患者存在高龄、合并症多、术后恢复慢等特点，常导致患者预后较差。研究表明，重度AS患者常伴有不同程度的二尖瓣关闭不全（mitral valve regurgitation，MR）^[1]，传统外科手术治疗通常会考虑同期双瓣膜修复/置换，但同期双瓣膜置换术又使高龄患者难以耐受。《2020 ACC/AHA心脏瓣膜病管理指南》建议，重度AS合并重度MR患者需要行同期双瓣膜置换术，但对于手术风险较高的患者可以考虑先行TAVR，后行择期心脏瓣膜介入治疗^[2]。国内外研究表明，TAVR对MR有改善作用^[3-4]。本研究旨在探讨二尖瓣反流面积（mitral regurgitation area，MRA）分级对重度AS合并MR患者TAVR后预后的影响，以期为该类患者临床治疗决策的制定提供参考。

1 对象与方法

1.1 研究对象 选取2018年4月至2021年7月在郑州市第七人民医院、河南省胸科医院应用自膨式瓣膜行TAVR的重度AS合并MR患者156例。纳入标准：（1）

重度AS患者，即超声心动图检查显示主动脉瓣瓣口面积 $<1.0 \text{ cm}^2$ ，或主动脉瓣上最大流速（maximum velocity on aortic valve，Vmax） $\geq 4.0 \text{ m/s}$ ，或主动脉瓣平均跨瓣压差 $\geq 40 \text{ mm Hg}$ （1 mm Hg=0.133 kPa）；（2）存在与AS相关的胸痛、晕厥、气促症状，且纽约心脏病协会（New York Heart Association，NYHA）分级 $\geq \text{II}$ 级；（3）影像学检查提示瓣膜植入部位解剖学上适合TAVR。排除标准：合并扩张型心肌病、主动脉夹层、感染性心内膜炎、风湿性二尖瓣病变、器质性二尖瓣病变、左心室流出道梗阻、左心室血栓及赘生物等不适合TAVR的患者。本研究已通过郑州市第七人民医院伦理委员会审核批准。

1.2 研究方法 查阅医院电子病历系统并收集患者的临床资料，包括性别、年龄、BMI、NYHA分级、合并症（包括高血压、糖尿病、冠心病、脑梗死、外周血管疾病、心房颤动、COPD、肺动脉高压、肾功能不全）发生情况、既往手术史及手术前后超声心动图检查结果〔包括升主动脉内径、左心室射血分数（left ventricular ejection fraction，LVEF）、左心室舒张末期内径（left ventricular end-diastolic diameter，LVEDD）、左心室收缩末期内径（left ventricular end-systolic diameter，LVESD）、室间隔

厚度 (interventricular septal thickness, IVST)、左心房内径 (left atrial diameter, LAD)、Vmax、主动脉瓣峰值跨瓣压差 (peak-aortic valve gradient, Peak-AVG)、MRA、MRA分级 (0级: MRA为0; 1级: MRA为 $1\sim4\text{ cm}^2$; 2级: MRA为 $>4\sim8\text{ cm}^2$; 3级: MRA $>8\text{ cm}^2$)]。所有患者术后1、6、12个月进行门诊或电话随访, 记录其主要不良心脑血管事件 (major adverse cardiac and cerebrovascular events, MACCE) 发生情况, 包括心力衰竭、心肌梗死、脑血管事件及心源性死亡。比较患者手术前后超声心动图检查结果, 有无MACCE患者性别、年龄、BMI、NYHA分级、合并症发生情况、既往手术史及术后超声心动图检查结果。

1.3 统计学方法 采用SPSS 26.0统计学软件进行数据处理。符合正态分布的计量资料以 $(\bar{x}\pm s)$ 表示, 两组间比较采用成组t检验, 组内比较采用配对t检验; 计数资料以 $[n(\%)]$ 表示, 组间比较采用 χ^2 检验; 等级资料比较采用Wilcoxon符号秩检验。重度AS合并MR患者TAVR后发生MACCE的影响因素分析采用多元Cox回归分析; 绘制ROC曲线以评估术后MRA分级对重度AS合并MR患者TAVR后发生MACCE的预测价值。以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 一般情况 156例患者均经股动脉路径行TAVR, 其中6例患者术中或术后24 h内死亡, 最终纳入150例患者。

2.2 患者手术前后超声心动图检查结果 术后患者升主动脉内径、LVEDD、LVESD、IVST、LAD、MRA小于术前, LVEF高于术前, Vmax慢于术前, Peak-AVG低于术前, MRA分级优于术前, 差异有统计学意义 ($P<0.05$), 见表1。

2.3 重度AS合并MR患者TAVR后发生MACCE的影响因素 随访12个月, 共32例患者发生MACCE, 其中心力衰竭13例、心肌梗死9例、脑血管事件10例。有无MACCE患者男性占比, 冠心病、脑梗死、外周血管疾病、COPD、肺动脉高压、肾功能不全发生率, 既往手术史, 术后升主动脉内径、Vmax、Peak-AVG比较,

差异无统计学意义 ($P>0.05$); 有无MACCE患者年龄、BMI、NYHA分级为Ⅲ~Ⅳ级者占比、高血压发生率、糖尿病发生率、心房颤动发生率及术后LVEF、LVEDD、LVESD、IVST、LAD、MRA分级 \geqslant 2级者占比比较, 差异有统计学意义 ($P<0.05$), 见表2。将表2中差异有统计学意义的指标 [年龄 (实测值), BMI (实测值), NYHA分级为Ⅲ~Ⅳ级 (赋值: 否=0, 是=1), 高血压 (赋值: 无=0, 有=1), 糖尿病 (赋值: 无=0, 有=1), 心房颤动 (赋值: 无=0, 有=1), 术后LVEF (实测值), 术后LVEDD (实测值), 术后LVESD (实测值), 术后IVST (实测值), 术后LAD (实测值), 术后MRA分级 (赋值: 0~1级=0, 2~3级=1)] 作为自变量, 是否发生MACCE作为因变量 (赋值: 未发生=0, 发生=1), 进行多元Cox回归分析, 结果显示, 术后LVEF、IVST、LAD、MRA分级是重度AS合并MR患者TAVR后发生MACCE的独立影响因素 ($P<0.05$), 见表3。

2.4 术后MRA分级对重度AS合并MR患者TAVR后发生MACCE的预测价值 ROC曲线分析结果显示, 术后MRA分级预测重度AS合并MR患者TAVR后发生MACCE的AUC为0.869 [95%CI (0.802, 0.935), $P<0.001$], 见图1。

3 讨论

本研究结果显示, 术后患者升主动脉内径、LVEDD、LVESD、IVST、LAD、MRA小于术前, LVEF高于术前, Vmax慢于术前, Peak-AVG低于术前, MRA分级优于术前, 提示TAVR可有效改善重度AS合并MR患者的心功能及减轻其二尖瓣反流程度, 与VIZZARDI^[5]研究结果一致。分析TAVR减轻重度AS合并MR患者二尖瓣反流程度的原因可能与AS解除后, 左心室流出道梗阻消失、二尖瓣跨瓣压及房室间压力梯度降低有关^[6~8]。因此, 对于高龄重度AS合并MR患者, 考虑到行同期双瓣膜置换术的风险较高, 可以先行TAVR治疗, 再根据二尖瓣反流改善情况决定是否行二尖瓣置换术。FREITAS-FERRAZ等^[9]进行的多中心研究结果显示, 术前合并中重度MR对AS患者4年全因

表1 患者手术前后超声心动图检查结果比较 (n=150)

Table 1 Comparison of echocardiography results of patients before and after operation

时间	升主动脉内径 ($\bar{x}\pm s$, mm)	LVEF ($\bar{x}\pm s$, %)	LVEDD ($\bar{x}\pm s$, mm)	LVESD ($\bar{x}\pm s$, mm)	IVST ($\bar{x}\pm s$, mm)	LAD ($\bar{x}\pm s$, mm)	Vmax ($\bar{x}\pm s$, m/s)	Peak-AVG ($\bar{x}\pm s$, mm Hg)	MRA ($\bar{x}\pm s$, cm^2)	MRA分级 [n (%)]			
										0级	1级	2级	3级
术前	38.5 ± 5.5	53.6 ± 13.6	50.4 ± 8.1	35.2 ± 8.1	13.9 ± 2.4	42.0 ± 6.2	4.9 ± 0.8	101.3 ± 27.1	5.8 ± 4.4	10 (6.7)	56 (37.3)	44 (29.3)	40 (26.7)
术后	36.0 ± 6.5	58.0 ± 10.5	46.9 ± 7.7	32.6 ± 7.6	13.0 ± 2.1	38.6 ± 5.5	2.0 ± 0.6	18.1 ± 8.7	3.2 ± 3.7	52 (34.7)	58 (38.7)	22 (14.7)	18 (12.0)
$t_{\text{配对}}(Z)$ 值	8.430	-6.185	10.010	6.861	5.051	7.642	42.496	42.240	12.080				-8.810 ^a
P值	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001				<0.001

注: ^a表示Z值; LVEF=左心室射血分数, LVEDD=左心室舒张末期内径, LVESD=左心室收缩末期内径, IVST=室间隔厚度, LAD=左心房内径, Vmax=主动脉瓣最大流速, Peak-AVG=主动脉瓣峰值跨瓣压差, MRA=二尖瓣反流面积

死亡率和心力衰竭再住院率无明显影响。KIRAMIJYAN等^[10]研究结果显示,术前伴有中度MR的AS患者术后30 d内死亡率较高〔HR=2.40, 95%CI(1.08, 5.29), P=0.031〕,但术前伴有中度MR对AS患者术后1年死亡

表2 有无MACCE患者性别、年龄、BMI、NYHA分级、合并症发生情况、既往手术史及术后超声心动图检查结果比较

Table 2 Comparison of gender, age, BMI, NYHA grading, complications, previous surgery history and postoperative echocardiography results between patients with MACCE and patients without MACCE

项目	无MACCE患者 (n=118)	有MACCE患者 (n=32)	t (χ ²) 值	P值
男性[n (%)]	70 (59.3)	20 (62.5)	0.106 ^a	0.745
年龄(̄±s, 岁)	73.1±6.3	76.2±5.9	2.365	0.019
BMI(̄±s, kg/m ²)	23.8±4.2	21.9±2.4	3.370	0.001
NYHA分级为Ⅲ~Ⅳ级 [n (%)]	88 (74.6)	32 (100.0)	10.169 ^a	0.001
合并症[n (%)]				
高血压	72 (61.0)	10 (31.3)	9.001 ^a	0.003
糖尿病	34 (33.3)	0	11.923 ^a	0.001
冠心病	48 (40.7)	14 (43.8)	0.098 ^a	0.754
脑梗死	20 (16.9)	8 (25.0)	1.075 ^a	0.300
外周血管疾病	26 (22.0)	4 (12.5)	1.430 ^a	0.232
心房颤动	10 (8.5)	8 (25.0)	5.039 ^a	0.025
COPD	6 (5.1)	0	0.629 ^a	0.428
肺动脉高压	6 (5.1)	4 (12.5)	1.192 ^a	0.275
肾功能不全	10 (8.5)	2 (6.3)	0.002 ^a	0.965
既往手术史[n (%)]				
冠状动脉支架植入术	10 (8.5)	0	1.703 ^a	0.192
瓣膜手术	2 (1.7)	0	0.550 ^a	0.458
术后超声心动图检查结果				
升主动脉内径(̄±s, mm)	35.6±5.8	37.6±8.1	1.338	0.188
LVEF(̄±s, %)	61.4±7.9	45.7±9.5	9.505	<0.001
LVEDD(̄±s, mm)	44.9±5.9	54.4±9.1	5.562	<0.001
LVESD(̄±s, mm)	30.2±5.4	41.6±7.9	7.683	<0.001
IVST(̄±s, mm)	13.5±1.9	11.2±1.7	6.072	<0.001
LAD(̄±s, mm)	37.5±4.4	42.4±7.3	3.756	<0.001
Vmax(̄±s, m/s)	2.0±0.6	2.0±0.7	0.086	0.931
Peak-AVG(̄±s, mm Hg)	18.4±9.1	16.7±7.1	1.012	0.313
MRA分级≥2级[n (%)]	18 (15.3)	22 (68.8)	36.839 ^a	<0.001

注: MACCE=主要不良心脑血管事件; ^a表示χ²值

表3 重度AS合并MR患者TAVR后发生MACCE影响因素的多元Cox回归分析

Table 3 Multivariate Cox regression analysis of influencing factors of MACCE after TAVR in severe AS patients with MR

变量	β	SE	Wald χ ² 值	P值	HR值	95%CI
术后LVEF	-0.076	0.022	11.890	0.001	0.927	(0.888, 0.968)
术后IVST	-0.684	0.169	16.320	<0.001	0.505	(0.362, 0.703)
术后LAD	0.170	0.051	11.061	0.001	1.185	(1.072, 1.309)
术后MRA 分级	1.205	0.557	4.671	0.031	3.336	(1.119, 9.946)

率无明显影响,分析该类患者术后30 d内死亡率较高的原因可能与其术后持续存在严重的MR增加了血流动力学恶化风险有关。FELDT等^[11]认为,与术前MR相比,MR的演变(如中重度MR持续、MR恶化)更能决定TAVR患者的远期死亡风险及不良事件发生风险,提示术后MR严重程度对TAVR患者的预后具有重要的预测价值。

本研究结果显示,术后LVEF、IVST、LAD、MRA分级是重度AS合并MR患者TAVR后发生MACCE的独立影响因素。研究表明,LVEF升高与心肌逆重构密切相关,如左心室肥厚和弥漫性纤维化减轻、左心舒张功能改善、左心室容积缩小等^[12-13]。WITBERG等^[3]研究发现,在术后MR持续存在的患者中,NYHA分级为Ⅲ~Ⅳ级者死亡率高于Ⅰ~Ⅱ级者(54.7%比29.6%,P<0.001),间接反映了术后LVEF对患者远期预后的影响。肥厚的间隔会导致流出道梗阻或左心室舒张功能受损^[14];而左心房又与左心室功能密切相关,左心房扩大患者心功能更差,且随着LVEF降低,左心室舒张压逐渐增高,左心房也逐渐增大,故LAD增大提示左心室前后负荷增加^[15]。研究表明,严重MR的持续存在会导致血流动力学恶化,增加左心室负荷,促进心力衰竭发生发展,进而导致患者预后不良^[16]。因此,尽早评估TAVR后MR严重程度对AS患者远期死亡及不良心脏事件的发生具有一定预测价值^[3, 8, 11]。AS患者TAVR后一旦发现其存在严重MR,应积极采取干预措施,如血运重建、心脏再同步化治疗及经导管二尖瓣介入治疗^[17-18],以提高患者的生存质量。本研究结果显示,术后MRA分级预测重度AS合并MR患者TAVR后

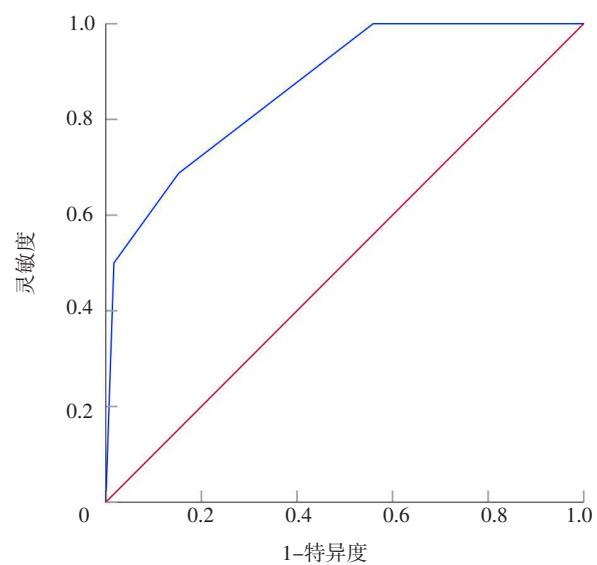


图1 术后MRA分级预测重度AS合并MR患者TAVR后发生MACCE的ROC曲线

Figure 1 ROC curve of postoperative MRA grading in predicting MACCE after TAVR in severe AS patients with MR

发生MACCE的AUC为0.869，提示术后MRA分级对重度AS合并MR患者TAVR后发生MACCE有一定预测价值。

综上所述，TAVR可有效改善重度AS合并MR患者的心功能及减轻其二尖瓣反流程度，术后MRA分级升高是重度AS合并MR患者TAVR后发生MACCE的危险因素，且其对患者TAVR后发生MACCE有较好的预测价值。但本研究样本量较小、随访时间较短，所得结论仍有待高质量研究进一步证实。

作者贡献：贺宇进行文章的构思与设计，结果分析与解释；牛毅菲、林振乾进行研究的实施与可行性分析；贺宇、牛毅菲、刘荣进行数据收集、整理、分析；贺宇、黄琼负责撰写、修订论文；袁义强负责文章的质量控制及审校，对文章整体负责、监督管理。

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