

• 临床研究 •

心肌瘢痕与药物治疗反应对非缺血性心肌病心衰患者室性心律失常风险的影响

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[摘要] 目的: 探究非缺血性心肌病(nonischemic cardiomyopathy, NICM)患者心肌瘢痕与药物治疗反应对室性心律失常发生风险的影响。方法: 回顾性分析在南京医科大学第一附属医院行心脏磁共振检查且接受药物治疗的77例左室射血分数(left ventricular ejection fraction, LVEF) $\leq 35\%$ 的NICM患者延迟钆增强(late gadolinium enhancement, LGE)与1年随访期内LVEF变化情况。采用Kaplan-Meier曲线和Log-rank检验进行生存分析, 多因素分析使用Cox比例风险回归。结果: 中位随访时间为34(16~49)个月。患者药物治疗后1年内LVEF变化与LGE无关($P=0.379$), 与LGE负荷呈负相关, 相关系数为 -0.295 (95%CI: $-0.487 \sim -0.076$, $P=0.009$)。随访期间, 5例患者发生室性快速心律失常(ventricular tachyarrhythmia, VTA)事件, 在生存分析中, VTA事件与LGE负荷有关($P=0.005$), 与LGE是否存在和药物治疗是否有反应无关($P=0.309$, $P=0.890$)。在多因素Cox回归模型中, LGE负荷是VTA事件的独立危险因素(HR=1.075, 95%CI: 1.002~1.054, $P=0.043$)。NICM患者远期复合终点与LGE负荷和LVEF变化有关($P=0.040$, $P=0.025$)。结论: LGE负荷是NICM患者发生VTA事件的独立危险因素, VTA事件的发生与药物治疗有无反应无关。

[关键词] 非缺血性心肌病; 左室射血分数; 心肌瘢痕; 延迟钆增强; 室性心律失常

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The impact of myocardial scarring and drug treatment response on the risk of ventricular arrhythmia in patients with nonischemic cardiomyopathy

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[Abstract] **Objective:** To investigate the impact of myocardial scarring and drug treatment response on the risk of ventricular arrhythmia in patients with nonischemic cardiomyopathy (NICM). **Methods:** A retrospective analysis was conducted on 77 NICM patients with left ventricular ejection fraction (LVEF) $\leq 35\%$ who underwent cardiac magnetic resonance with late gadolinium enhancement (LGE) and received drug therapy at the First Affiliated Hospital of Nanjing Medical University. The changes in LVEF during the one-year follow-up period were collected. Kaplan-Meier curves and Log-rank tests were used for survival analysis, and multivariate analysis was performed using Cox proportional hazards regression. **Results:** The median follow-up time was 34 (16–49) months. Changes in LVEF within one year after drug treatment were not related to LGE ($P=0.379$), but were negatively correlated with LGE burden, with a correlation coefficient of -0.295 (95% CI: $-0.487 \sim -0.076$, $P=0.009$). During follow-up, five patients experienced ventricular tachyarrhythmia (VTA) events. In survival analysis, VTA events were associated with LGE burden ($P=0.005$) but were not related to the presence of LGE or drug treatment response ($P=0.309$, $P=0.890$). In the multivariate Cox regression model, LGE burden was an independent risk factor of VTA events (HR=1.075, 95% CI: 1.002–1.054, $P=0.043$). The long-term composite endpoint of NICM patients was related to LGE burden and LVEF changes ($P=0.040$, $P=0.025$). **Conclusion:** LGE burden is an independent risk factor for the occurrence of VTA events in NICM patients, and the occurrence of VTA events is not related to drug treatment response.

[Key words] nonischemic cardiomyopathy; left ventricular ejection fraction; myocardial scarring; late gadolinium enhancement; ventricular arrhythmia

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非缺血性心肌病(nonischemic cardiomyopathy, NICM)是一种由于非冠状动脉粥样硬化导致的心脏结构和/或功能不全而引发的心源性心力衰竭。NICM患者心肌收缩能力受损,易发生室性心律失常,进而诱发心源性猝死(sudden cardiac death, SCD)^[1],目前,NICM约占SCD病因的20%^[2]。左心室射血分数(left ventricular ejection fraction, LVEF)被广泛应用于SCD的风险评估^[3],但预测价值有限^[4]。近年来,人们越来越关注心脏磁共振(cardiac magnetic resonance, CMR)延迟钆增强(late gadolinium enhancement, LGE)所代表的心肌瘢痕对室性心律失常的影响。先前研究表明,心肌瘢痕的存在、表现和特征可用于预测缺血性心肌病(ischemic cardiomyopathy, ICM)和NICM^[5-8]的心律失常事件,因此可用于筛选心律失常风险增加的患者,这些患者将更大程度地从植入式心脏转复除颤器(implantable cardioverter defibrillator, ICD)治疗中受益^[9],而一些接受药物治疗后的NICM患者可能由于LVEF的提升而失去ICD的植入指征,故本研究旨在探究NICM患者心肌瘢痕与药物治疗反应对室性心律失常风险的影响。

1 对象和方法

1.1 对象

回顾性分析2018年5月—2023年2月在南京医科大学第一附属医院行CMR检查的NICM患者,纳入标准:①基线LVEF $\leq 35\%$;②未接受器械植入;③存在至少1次1年内LVEF随访数据;④年龄 ≥ 18 周岁且 < 80 周岁。排除标准:①临床数据缺失或CMR图像不全及质量不佳;②有心肌炎、肥厚型心肌病、致心律失常型右室心肌病、严重瓣膜病、浸润性疾病和ICM病史,ICM被定义为血管造影时心外膜冠状动脉存在 $\geq 70\%$ 的管腔狭窄,无创应力成像提示缺血或既往心肌梗死;③有记录在案的持续性室性心动过速(ventricular tachycardia, VT)、心室颤动(ventricular fibrillation, VF)或心脏骤停复苏病史。在连续纳入的112例慢性心衰并接受CMR检查的患者中,排除6例严重瓣膜病、21例ICM和8例失访患者后,最终共纳入77例患者。本研究符合《赫尔辛基宣言》原则,鉴于回顾性研究,患者知情同意书已被免除。

1.2 方法

1.2.1 CMR扫描

CMR通过3.0T系统完成(SkyraandVida, Siemens Healthcare公司,德国)。CMR序列:①电影序

列,平衡稳态自由进动序列通过屏气来获得左心室长轴位(二腔、三腔及四腔)和短轴电影图像;②延迟增强,采用相位敏感反转恢复(phase sensitive inversion recovery, PSIR)序列LGE成像,主要参数:视野340~380 mm,重复时间/回声时间:44.8 ms/1.4 ms,矩阵208 mm $\times$ 188 mm,体素1.6 mm $\times$ 1.6 mm $\times$ 8.0 mm,带宽962 Hz/Px,反转角47°,层厚8 mm,层间距2 mm。以0.2 mmol/kg的剂量静脉给予钆喷酸葡胺(Gd-DTPA,马根维显,拜耳公司,德国),10~15 min后进行LGE扫描。

1.2.2 图像分析

所有图像分析都使用CMR图像后处理软件(Circle CVI-42、Circle Cardiovascular Imaging, Calgary公司,加拿大)。通过勾画左心室短轴位电影图像的心内膜与心外膜轮廓,计算左心室的心功能参数,包括舒张末期容积、收缩末期容积、每搏输出量、左心室每分输出量以及左心室心肌质量,并且对于上述参数进行体表面积标化,从而计算出LVEF。如果在长轴和短轴平面上、在两个相位编码方向上观察到LGE,并且延伸到局部右心室插入区域之外,则认为存在LGE^[10]。测量感兴趣区域的平均信号强度和标准差,并将心肌纤维化定义为信号强度高于正常心肌信号5个标准差的心肌^[11]。LGE负荷定义为延迟强化的心肌质量占总心肌质量的百分比,LGE分析由2名对临床信息不知情的独立观察者进行。

1.2.3 随访数据收集

收集患者基线与1年随访期间的二维超声心动图LVEF值,其中,对药物治疗有反应定义为治疗1年后的LVEF提升 $\geq 10\%$ 。中位随访时间34(16~49)个月,随访方式为门诊、住院定期复查或电话随访,以判断结局终点是否发生。

1.2.4 结局

主要结局终点是复合的室性快速心律失常(ventricular tachyarrhythmia, VTA)事件,其定义为持续性VT、VF、SCD、心脏骤停后的复苏;持续性VT是指心率 ≥ 100 次/min、持续时间 ≥ 30 s或需要干预终止的心动过速。SCD被定义为“由于各种心脏原因引起的非暴力自然死亡,在急性症状出现后1 h内突然出现意识丧失、引起意外的死亡”。次要结局为VTA、全因死亡及心衰再住院(heart failure hospitalization, HFH)的远期复合终点。

1.3 统计学方法

应用SPSS26.0与GraphPad 9.0.0软件进行统计

学分析,计数资料用例数(百分比)[$n(\%)$]表示,通过卡方检验或 Fisher 精确检验进行组间差异比较。定量资料先行正态性检验,正态分布指标以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,采用独立样本 t 检验进行组间比较;非正态分布指标以中位数(四分位数)[$M(P_{25}, P_{75})$]表示,组间比较采用 Mann-Whitney U 检验。采用相关性分析确定 LGE 与 LVEF 变化的相关性,通过 Kaplan-Meier 法估计患者的 VTA 发生率,不同亚组间的生存比较使用 Log-rank 检验。采用 Cox 比例风险回归模型确定 VTA 的独立危险因素。绘制受试者工作特征(receiver operating characteristics, ROC)曲线,通过计算曲线下面积(area under the curve, AUC)确定诊断效能,根据最大约登指数建立预测结局终点的最佳阈值, $P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 临床基线资料

最终 77 例 NICM 患者纳入分析,年龄(49.8 ± 14.0)岁,其中,男 57 例(74.0%),6 例(7.8%)左束支传导阻滞,基线 LVEF 为(29.9 ± 5.7)%,左心室舒张末期容积(left ventricular end - diastolic volume, LVEDV)(295.1 ± 100.6)mL,65 例(84.4%)存在 LGE, LGE 中位负荷为 3.6%(1.2%,9.5%), Δ LVEF 中位数为 13.6%(2.8%,22.7%)。患者的临床基线特征见表 1。

2.2 药物治疗反应

在 1 年随访期中,44 例(57.1%)患者 LVEF 提升 $\geq 10\%$,18 例(23.3%)患者 LVEF 超过 40%,29 例(37.7%)患者 LVEF 超过 50%。LGE 是否存在与 Δ LVEF 之间无相关性($P=0.379$),LGE 负荷与患者药物治疗后 1 年 LVEF 变化呈负相关(图 1),相关系数为 -0.295 (95%CI: $-0.487 \sim -0.076$, $P=0.009$)。

2.3 临床结局终点

在中位随访时间 34(16~49)个月中,共发生 5 例 VTA 事件,仅存在于 LGE 阳性患者中,而在有反应与无反应组中皆有发生,且 5 例患者 1 年随访时的 LVEF 均 $>50\%$ 。Kaplan-Meier 分析显示,LGE 负荷越大(cut-off=5.78%),VTA 事件发生率越高($P=0.005$),而 LGE 是否存在($P=0.309$)与药物治疗有无反应($P=0.890$)在两组 VTA 事件的发生率上差异无统计学意义(图 2)。将基线中的各项指标纳入单因素回归模型,结果表明 LGE 负荷是 VTA 事件的预测因子($HR=1.052$,95%CI: 1.004~1.101, $P=0.033$),而药物治疗有无反应和 Δ LVEF 皆与 VTA 事件的发生无关($P=0.891$, $P=0.613$,表 2)。将 LGE 负荷与药物治疗

表 1 患者的基线特征
Table 1 Baseline characteristics of the patients
($n=77$)

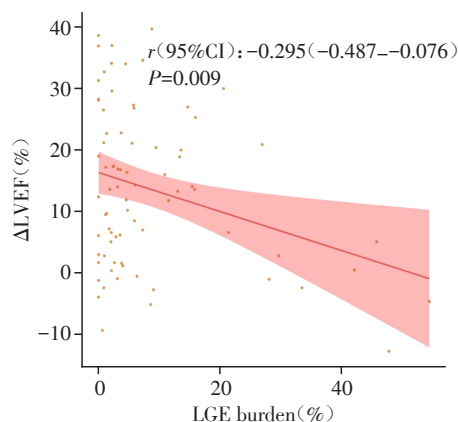
Variable	Value
Age(years, $\bar{x} \pm s$)	49.8 $\pm$ 14.0
Male[$n(\%)$]	57(74.0)
BSA(m ² , $\bar{x} \pm s$)	1.84 $\pm$ 0.24
Diabetes mellitus[$n(\%)$]	9(11.7)
Arterial hypertension[$n(\%)$]	33(42.9)
HR(beats/min, $\bar{x} \pm s$)	78.1 $\pm$ 17.6
AF[$n(\%)$]	11(14.3)
LBBB[$n(\%)$]	6(7.8)
QRS(ms, $\bar{x} \pm s$)	112.0 $\pm$ 21.9
NYHA($\bar{x} \pm s$)	2.8 $\pm$ 0.7
LVEF(% , $\bar{x} \pm s$)	29.9 $\pm$ 5.7
LVEDV(mL, $\bar{x} \pm s$)	295.1 $\pm$ 100.6
LVESV(mL, $\bar{x} \pm s$)	229.8 $\pm$ 91.1
LVM(g, $\bar{x} \pm s$)	208.2 $\pm$ 65.6
ACEI/ARB/ARNI[$n(\%)$]	54(70.1)
Beta-blocker[$n(\%)$]	72(93.5)
MRA[$n(\%)$]	63(81.8)
SGLT2i[$n(\%)$]	30(39.0)
Diuretic[$n(\%)$]	57(74.0)
NT-proBNP[ng/L, $M(P_{25}, P_{75})$]	1 609.0(567.0, 2 905.6)
LGE[$n(\%)$]	65(84.4)
LGE burden[% , $M(P_{25}, P_{75})$]	3.6(1.2, 9.5)
Δ LVEF[% , $M(P_{25}, P_{75})$]	13.6(2.8, 22.7)

BSA: bodysurface area; HR: heart rate; AF: atrial fibrillation; LBBB: left bundle branch block; NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolicvolume; LVM: left ventricular mass; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor neprilysin inhibitor; MRA: mineralocorticoid receptor antagonist; SGLT2i: sodium-glucose cotransporter-2 inhibitor; NT-proBNP: N-terminal pro-brain natriuretic peptide.

有无反应纳入多因素回归分析,结果提示 LGE 负荷是 VTA 事件的独立危险因素($HR=1.075$,95%CI: 1.002~1.154, $P=0.043$,表 3)。

在药物治疗有反应的 44 例中进行亚组分析, Kaplan-Meire 分析提示在该人群中 LGE 负荷仍然与 VTA 事件发生有关, LGE 负荷越大, VTA 事件发生率越高($P=0.024$,图 3)。

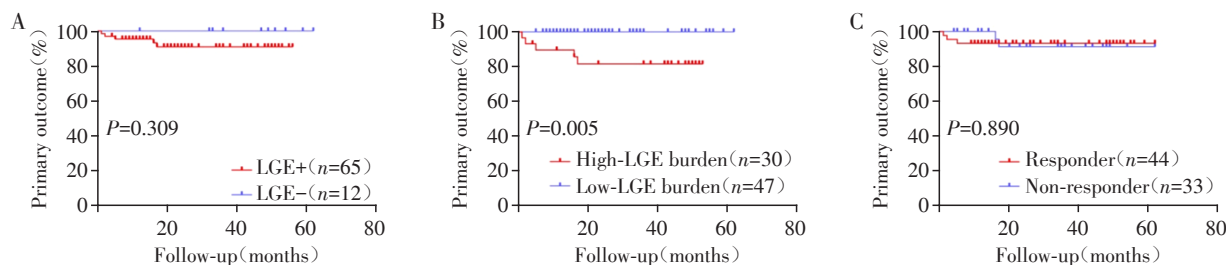
在随访期内,共有 17 例远期复合终点发生,包括 6 例全因死亡与 8 例 HFH, Cox 单因素分析提示 LGE 负荷($HR=1.031$,95%CI: 1.001~1.062, $P=0.040$)与 Δ LVEF($HR=0.954$,95%CI: 0.915~0.994, $P=0.025$)与远期复合终点有关(表 4)。



Change in LVEF by drug therapy according to LGE burden in patients (red dots). $r = -0.295$, 95% CI: -0.487 – -0.076 , $P = 0.009$. LVEF: left ventricular ejection fraction; LGE: late gadolinium enhancement.

图1 不同LGE负荷患者的 Δ LVEF散点图

Figure 1 Scatter plot of Δ LVEF in patients with different LGE burden



A: Kaplan-Meier curves for VTA events stratified by LGE status are presented. The LGE-positive group (red curve) and the LGE-negative group (blue curve) demonstrated comparable outcomes (Log-rank $P = 0.309$). B: Kaplan-Meier analysis of VTA events categorized by LGE burden using a cut-off value of 5.78, is illustrated. The high LGE burden group (>5.78 , red curve) showed significantly worse prognosis compared to the low burden group (<5.78 , blue curve) (Log-rank $P = 0.005$). C: Therapeutic response analysis displayed, with drug responsive patients (Δ LVEF $\geq 10\%$, red curve) and non-responders (Δ LVEF $< 10\%$, blue curve) showing comparable VTA event rates (Log-rank $P = 0.890$).

图2 VTA事件的生存分析

Figure 2 Kaplan-Meier curves for VTA

事件的发生率都明显升高,且LGE阳性患者发生左室逆重构(left ventricular reverse remodeling, LVRR)的概率也越小^[12]。Ota等^[13]探究了不同LGE模式对NICM患者LVRR频率的影响,研究发现,相比LGE阴性组与中壁LGE组,多发LGE病变组的LVRR频率明显更低。本研究进一步探究了不同LGE负荷与 Δ LVEF的关系,LGE负荷越大, Δ LVEF越小,心功能改善越差。在大多数情况下,室速发生于传导缓慢和单向阻滞的区域,这些区域并不都存在于LVEF降低的患者中,但都存在心肌瘢痕。既往研究表明,心肌瘢痕是VTA的一个强有力的预测因子^[7-8, 14-17]。Halliday等^[18]研究发现,对于LVEF轻度和中度降低的扩张型心肌病患者,尽管不是ICD一级预防的适应证,但通过磁共振检测发现中层心肌延迟强化可以识别其中的高危人群。这些与本研究结论中

3 讨论

本研究的主要发现是LVEF降低的NICM患者室性心律失常事件的发生与LGE负荷有关,与LGE是否存在和药物治疗有无反应无关。

恶性心律失常引起的SCD是NICM发生致死性结局的主要原因之一,目前指南推荐在LVEF $\leq 35\%$ 的患者中植入ICD进行SCD的一级预防,但LVEF识别SCD风险的特异度及灵敏度都相对较低,另一方面,SCD也可能发生在LVEF正常或轻度降低的人群中^[4]。因此,有必要确定新的标志物来改善SCD的危险分层。越来越多的研究表明,心肌瘢痕与NICM患者的不良预后有关,一项纳入了4 554例患者的Meta分析显示,相比LGE阴性的患者,LGE阳性患者无论是心血管死亡、VTA或是心衰再住院

LGE负荷是VTA事件的独立危险因素相符,但有趣的是,本研究中VTA事件发生与LGE是否存在无关,只与LGE的负荷大小有关。本课题组之前的研究探究了LGE不同模式与NICM患者VTA事件的关系,结果表明环状LGE对VTA事件的预测价值最大,风险比最高^[19]。在一项关于机械不同步参数联合室间隔LGE预测心衰患者心脏再同步化治疗(cardiac resynchronization therapy, CRT)效果的研究中,相比其他部位,只有室间隔部位的LGE是心室逆重构的独立危险因素^[20]。因此,推测不同部位的LGE对VTA事件的预测价值不同可能是本研究中LGE与VTA事件无关的原因。Linhart等^[21]发现VTA事件发生的可能性与瘢痕质量存在剂量依赖效应,VTA事件发生的概率随着瘢痕质量的增加而增加,这与本课题组之前研究发现的VTA事件与

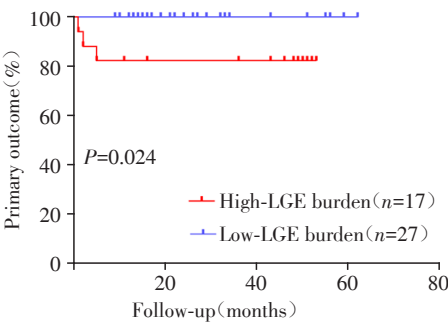
表2 VTA事件的Cox单因素分析
Table 2 Univariate Cox regression analysis for VTA

Variable	Primary event(n=5)	No primary event(n=72)	HR(95%CI)	P
Age(years, $\bar{x} \pm s$)	47.2 $\pm$ 6.2	49.9 $\pm$ 14.4	0.989(0.928-1.054)	0.730
Male[n(%)]	5(100.0)	52(72.2)	-	0.199*
BSA(m ² , $\bar{x} \pm s$)	1.78 $\pm$ 0.13	1.85 $\pm$ 0.25	0.275(0.004-17.763)	0.544
Diabetes mellitus[n(%)]	0(0)	9(2.5)	-	0.487*
Arterial hypertension[n(%)]	1(20.0)	32(44.4)	0.322(0.036-2.884)	0.311
AF[n(%)]	1(20.0)	1(13.9)	1.820(0.201-16.513)	0.595
LBBB[n(%)]	0(0)	6(8.3)	-	0.515*
NYHA($\bar{x} \pm s$)	3.2 $\pm$ 0.8	2.7 $\pm$ 0.7	2.481(0.638-9.651)	0.190
LVEF(% , $\bar{x} \pm s$)	31.8 $\pm$ 5.4	29.8 $\pm$ 5.7	1.081(0.915-1.278)	0.358
LVEDV(mL, $\bar{x} \pm s$)	299.6 $\pm$ 123.7	294.8 $\pm$ 99.8	1.000(0.992-1.009)	0.929
LVESV(mL, $\bar{x} \pm s$)	238.8 $\pm$ 107.1	229.1 $\pm$ 90.7	1.001(0.992-1.010)	0.832
LVM(g, $\bar{x} \pm s$)	180.9 $\pm$ 38.7	210.0 $\pm$ 66.8	0.993(0.979-1.007)	0.332
ACEI/ARB/ARNI[n(%)]	3(60.0)	51(70.8)	0.575(0.096-3.445)	0.544
Beta blocker[n(%)]	4(80.0)	68(94.4)	0.284(0.032-2.539)	0.260
MRA[n(%)]	5(100.0)	58(80.6)	-	0.306*
Diuretics[n(%)]	4(80.0)	53(73.6)	1.377(0.154-12.323)	0.775
SGLT2i[n(%)]	0(0)	30(41.7)	-	0.095*
NT-proBNP[ng/L, $M(P_{25}, P_{75})$]	2 667.0(2 603.0, 9 000.0)	1 464.0(549.5, 2 818.9)	1.000(1.000-1.000)	0.271
LGE[n(%)]	5(100.0)	60(83.3)	-	0.309*
LGE burden[% , $M(P_{25}, P_{75})$]	21.2 $\pm$ 15.6	7.5 $\pm$ 11.2	1.052(1.004-1.101)	0.033
Δ LVEF[% , $M(P_{25}, P_{75})$]	11.8(0.5, 18.9)	13.6(3.0, 22.7)	0.982(0.914-1.055)	0.613
Drug response[n(%)]	3(60.0)	41(56.9)	1.134(0.189-6.786)	0.891

*: Due to a group of no outcome events occurring in this categorical variable, the P-value here is calculated using the Log-rank test.

表3 VTA事件的Cox多因素分析
Table 3 Multivariate Cox regression analysis for VTA

Variable	HR(95%CI)	P
Drug response	3.678(0.269-50.323)	0.329
LGE burden	1.075(1.002-1.154)	0.043



Kaplan-Meier analysis of LGE burden and VTA events in drug responsive patients (n=44). Using a cut-off value of 5.78, the high LGE burden group(>5.78, red curve) demonstrated significantly higher event rates compared to the low burden group(<5.78, blue curve), with a Log-rank P value of 0.024.

图3 药物治疗有反应人群的亚组分析

Figure 3 Subgroup analysis of drug responders

LGE负荷大小相关一致。

本研究纳入的是LVEF≤35%的接受药物治疗的NICM患者,他们往往处于一种特殊情况中,由于降低的LVEF是目前ICD植入一级预防的标准,然而心衰药物治疗通过调节神经体液机制逆转左室重构,改善LVEF,许多患者逐渐超过了ICD植入的阈值,在该人群中,ICD植入的有效性尚不清楚。Linhart等^[21]研究发现VTA与心衰患者CRT植入1年之后的逆重构无关,在Van Der等^[22]的研究中,有23%的CRT超反应者接受了恰当的ICD治疗,虽然CRT逆转左室重构,提升LVEF是通过改善心脏机械同步性实现的,与药物治疗通过调节神经体液机制提升LVEF不同,但患者心功能的好转与是否发生VTA无关却与本研究结论相符。

本研究的局限性在于这是一项回顾性研究,样本量较少,结局终点发生数少,由于在本中心行磁共振检查的患者大多症状较重,且心脏扩大明显(LVEDV=295.1 mL),LVEF明显降低(29.9%),故队列LGE阳性的比例比一般NICM人群高(84.0%),且

表4 远期复合终点的Cox单因素分析

Table 4 Univariate Cox regression analysis for long term composite endpoint

Variable	Secondary event(n=17)	No secondary event(n=60)	HR(95%CI)	P
Age(years, $\bar{x} \pm s$)	46.6 $\pm$ 12.0	50.7 $\pm$ 14.5	0.982(0.949–1.017)	0.307
Male[n(%)]	14(82.4)	43(71.7)	1.700(0.488–5.918)	0.405
BSA(m ² , $\bar{x} \pm s$)	1.85 $\pm$ 0.22	1.84 $\pm$ 0.25	1.158(0.148–9.026)	0.889
Diabetes mellitus[n(%)]	0(0)	9(15.0)	–	0.209*
Arterial hypertension[n(%)]	6(35.3)	27(45.0)	0.617(0.227–1.677)	0.344
AF[n(%)]	2(11.8)	9(15.0)	1.086(0.246–4.795)	0.913
LBBB[n(%)]	0(0)	6(10.0)	–	0.913*
NYHA($\bar{x} \pm s$)	3.0 $\pm$ 0.7	2.7 $\pm$ 0.7	1.675(0.792–3.539)	0.177
LVEF(% , $\bar{x} \pm s$)	29.0 $\pm$ 6.0	30.2 $\pm$ 5.6	0.988(0.904–1.079)	0.782
LVEDV(mL, $\bar{x} \pm s$)	341.3 $\pm$ 129.0	282.0 $\pm$ 87.9	1.006(1.002–1.010)	0.007
LVESV(mL, $\bar{x} \pm s$)	274.6 $\pm$ 119.3	217.0 $\pm$ 78.0	1.007(1.002–1.011)	0.005
LVM(g, $\bar{x} \pm s$)	205.5 $\pm$ 82.0	208.9 $\pm$ 60.9	0.999(0.991–1.007)	0.810
ACEI/ARB/ARNI[n(%)]	11(64.7)	43(71.7)	0.814(0.300–2.210)	0.687
Beta blocker[n(%)]	15(88.2)	57(95.0)	0.434(0.099–1.907)	0.269
MRA[n(%)]	15(88.2)	48(80.0)	1.304(0.295–5.762)	0.726
Diuretics[n(%)]	13(76.5)	44(73.3)	0.964(0.313–2.966)	0.949
SGLT2i[n(%)]	2(11.8)	28(46.7)	0.321(0.071–1.443)	0.138
NT-proBNP[ng/L, $M(P_{25}, P_{75})$]	2 667.0(653.0, 8 680.0)	1 296.5(495.0, 2 615.0)	1.000(1.000–1.000)	0.231
LGE[n(%)]	14(82.4)	51(85.0)	1.133(0.324–3.966)	0.845
LGE burden[% , $M(P_{25}, P_{75})$]	9.0(1.0, 28.1)	3.1(1.3, 7.3)	1.031(1.001–1.062)	0.040
Δ LVEF[% , $M(P_{25}, P_{75})$]	29.0 $\pm$ 6.0	14.1(6.2, 23.4)	0.954(0.915–0.994)	0.025
Drug response[n(%)]	7(41.2)	37(61.7)	0.498(0.189–1.310)	0.158

*: Due to a group of no outcome events occurring in this categorical variable, the *P*-value here is calculated using the Log-rank test.

对患者用药是否符合心衰标准化药物治疗未作进一步统计分析,许多心衰药物具有抗纤维化作用,包括β受体阻滞剂、血管紧张素转换酶抑制剂及钠葡萄糖共转运蛋白2抑制剂等^[23–24]。本研究纳入患者使用药物的比例在发生与未发生结局终点两组之间差异无统计学意义,因此不同的药物联合LGE对NICM患者远期预后的影响有待进一步确认。

综上,采用CMR评估的LGE负荷与NICM患者药物治疗后LVEF提升呈负相关,且LGE负荷是NICM患者VTA事件的独立危险因素,VTA事件与药物治疗反应无关。

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所有作者声明无利益冲突。

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作者贡献声明:
计雨佳、张恩瑞、张新尉共同参与了研究思路的设计;计雨佳、张新尉进行数据收集与分析;张恩瑞负责图表制作;计雨佳撰写论文。

Author’s Contributions:
JI Yujia, ZHANG Enrui, and ZHANG Xinwei contributed

to the research design; JI Yujia and ZHANG Xinwei collected and analyzed the data; ZHANG Enrui was responsible for preparing the charts; JI Yujia wrote the manuscript.

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