

· 老年人心律失常专栏 ·

年龄对阵发性心房颤动终止后长间歇患者窦房结功能的影响

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【摘要】目的 探讨年龄对阵发性心房颤动(房颤)终止后出现长间歇的患者窦房结功能的影响。**方法** 连续入选2011年5月至2013年5月于我院就诊的358例接受射频消融术的阵发性房颤患者, 年龄(63 ± 11)岁, 男220例, 女138例。根据年龄将其分为两组: 即非老年组(年龄 < 65 岁, $n = 177$)及老年组(年龄 ≥ 65 岁, $n = 181$)。比较两组患者术前长间歇的检出率及术后窦房结功能的恢复率。**结果** 老年阵发性房颤患者术前更易出现提示窦房结功能障碍的房颤终止后长间歇, 其检出率显著高于非老年组(14.4% vs 5.6%, $P < 0.01$)。术后随访(15.0 ± 8.7)个月, 非老年组的窦房结功能障碍检出率显著低于术前(1.1% vs 5.6%, $P < 0.05$), 而老年组仅有降低趋势(9.4% vs 14.4%, $P > 0.05$)。老年患者术后窦房结功能的好转率显著低于非老年患者(34.6% vs 80.0%, $P < 0.05$)。**结论** 年龄对阵发性房颤终止后出现长间歇患者的窦房结功能评价具有重要价值。老年房颤患者经射频消融术治疗后, 多数窦房结功能无明显改善, 常须植入永久起搏器治疗。

【关键词】 心房颤动; 年龄因素; 导管消融术; 窦房结功能障碍

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Impact of age on sinus node function in patients with prolonged sinus pauses after termination of paroxysmal atrial fibrillation

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【Abstract】 Objective To determine the impact of age on the sinus node function in the patients with prolonged sinus pauses after termination of paroxysmal atrial fibrillation (PAF). **Methods** A total of 358 consecutive PAF patients with age of (63 ± 11) years (220 males and 138 females) who received radiofrequency ablation in our department from May 2011 to May 2013 were enrolled in this study. They were divided into 2 groups: older group ($n = 181$, ≥ 65 years old) and non-older group ($n = 177$, < 65 years old). The prevalence of prolonged sinus pauses before the ablation and the rate of sinus node functional restoration after procedure were compared between the 2 groups. **Results** The older patients tended to have higher prevalence of prolonged sinus pauses after termination of PAF (indicating sinus node dysfunction) than non-older patients (14.4% vs 5.6%, $P < 0.01$). After the follow-up of (15.0 ± 8.7) months, the prevalence of sinus node dysfunction was significantly lower than before catheter ablation in non-older group (1.1% vs 5.6%, $P < 0.05$). But there was only a decreasing trend in older patients (9.4% vs 14.4%, $P > 0.05$). The rate of sinus node functional restoration was significantly lower in older patients than in non-older ones, (34.6% vs 80.0%, $P < 0.05$). **Conclusion** Age plays an important role in the evaluation of sinus node function in patients with prolonged sinus pauses after termination of PAF. For the elderly patients with PAF, radiofrequency ablation exerts no obvious effect on sinus node function, and permanent pacemaker implantation is recommended in this situation.

【Key words】 atrial fibrillation; age factors; catheter ablation; sinus node dysfunction

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阵发性心房颤动(房颤)发作终止后出现长间歇的患者在临床上较为常见。但这些患者是否存在器质性窦房结功能障碍目前尚存争议。有研究表明,大部分合并阵发性房颤终止后长间歇的患者在经过成功的射频消融治疗后,其长间歇可消失,从而无需植入永久起搏器治疗^[1,2]。然而,临床实践表明,阵发性房颤发作后的长间歇在病理生理层面具有非均质性,部分患者即使在成功消融房颤后,其窦房结功能障碍未见改善,仍需植入永久起搏器,且多见于老年人。鉴于此,本研究旨在探讨年龄对阵发性房颤终止后长间歇患者窦房结功能的影响。

1 对象与方法

1.1 研究对象

连续入选2011年5月至2013年5月就诊于首都医科大学附属北京朝阳医院房颤中心明确诊断为阵发性房颤的患者358例,年龄(63 ± 11)岁,其中男性220例(61.5%),女性138例(38.5%),239例(66.8%)合并高血压,80例(22.3%)合并器质性心脏病。依据年龄,将入选患者分为两组:非老年组(年龄 < 65 岁, $n = 177$)及老年组(年龄 ≥ 65 岁, $n = 181$)。患者均行房颤射频消融治疗。房颤终止后长间歇的定义:经动态心电图或其他心电监测手段证实,在房颤发作终止后随之出现 $\geq 3s$ 的RR长间歇;或虽无心电学证据,但患者在房颤终止瞬间出现晕厥或者几乎晕厥者。术前在两次房颤发作间期已经被诊断为病态窦房结综合征的患者除外。详细基线资料见表1,表2。

1.2 射频消融策略

房颤患者均在三维电解剖标测(CARTO)系统指导下行环肺静脉电隔离术。消融终点为两侧肺静脉电学隔离。完成预设消融线后采用环状标测导管(LassoTM, Biosense-Webster, USA)分别验证各肺静脉是否达到电学隔离,必要时补充消融,直至肺静脉完全隔离。隔离肺静脉并至少观察20min后,先后静脉注射异丙肾上腺素和腺苷三磷酸诱发肺静脉外局灶触发的房颤,并评估肺静脉电传导恢复率。对于诱发阳性者给予补充消融,直至诱发试验阴性。

1.3 术后观察及随访

术后对所有患者行心电遥测至少24h,同时继续服用一种Ⅲ类或者Ⅰc类抗心律失常药物(antiarrhythmic drug, AAD)3个月。出院后所有患者定期于第1, 3, 6个月时复查24h动态心电图,之后每隔半年复查1次。对于术前即存在阵发性房颤发作终止后长间歇的患者同时应用触发式电话心电图进行为期3个月的随访。在随访过程中若患者出现心悸、头晕、黑矇、晕厥等不适症状时亦及时复查动态心电图。器质性窦房结功能障碍定义为窦性心律时,停用AAD后动态心电图仍提示有窦性停搏RR间期 $> 3s$ 。房颤复发定义为术后3个月停用AAD后,记录到持续时间 $\geq 30s$ 的快速性房性心律失常。

1.4 分析指标

比较非老年组及老年组患者的临床资料、术前阵发性房颤发作终止后长间歇的检出率、术后器质

表1 入选358例房颤患者的基线资料
Table 1 Baseline data of 358 patients with AF

Subjects	n	Females [n(%)]	History of AF (months)	Hypertention [n(%)]	SHD [n(%)]	LAD (mm, $\bar{x} \pm s$)	LVEF (%, $\bar{x} \pm s$)	BNP (ng/L, $\bar{x} \pm s$)
Total sample	358	138 (38.5)	12 (6-36)	239 (66.8)	80 (22.3)	34 $\pm$ 13	62 $\pm$ 18	781 $\pm$ 1511
Non-older group	177	58 (32.8)*	12 (6-36)	94 (53.1)***	28 (15.8)***	34 $\pm$ 13	61 $\pm$ 20	494 $\pm$ 940***
Older group	181	80 (44.2)	12 (8-36)	145 (80.1)	52 (28.7)	35 $\pm$ 12	64 $\pm$ 18	1066 $\pm$ 1 878

AF: atrial fibrillation; SHD: structural heart disease, including hypertrophic cardiomyopathy and coronary atherosclerotic cardiopathy; LAD: left atrial diameter; LVEF: left ventricular ejection fraction; BNP: brain natriuretic peptide. Compared with older group, * $P < 0.05$, *** $P < 0.001$

表2 术前合并房颤发作终止后长间歇患者的基线资料
Table 2 Baseline data of patients with prolonged sinus pauses after termination of AF

Subjects	n	Females [n(%)]	History of AF (months, $\bar{x} \pm s$)	Hypertention [n(%)]	SHD [n(%)]	LAD (mm, $\bar{x} \pm s$)	LVEF (%, $\bar{x} \pm s$)	BNP (ng/L, $\bar{x} \pm s$)
Total sample	36	13 (36.1)	45 $\pm$ 64	23 (63.4)	11 (30.6)	33 $\pm$ 13	61 $\pm$ 21	1173 $\pm$ 1622
Non-older group	10	3 (30.0)	48 $\pm$ 48	5 (50.0)	2 (20.0)	32 $\pm$ 15	58 $\pm$ 27	832 $\pm$ 1 479
Older group	26	10 (38.5)	44 $\pm$ 42	18 (69.2)	9 (34.6)	33 $\pm$ 13	63 $\pm$ 20	1269 $\pm$ 1677

AF: atrial fibrillation; SHD: structural heart disease, including hypertrophic cardiomyopathy and coronary atherosclerotic cardiopathy; LAD: left atrial diameter; LVEF: left ventricular ejection fraction; BNP: brain natriuretic peptide

性窦房结功能障碍阳性率、术后窦房结功能好转率等。对两组患者术前与术后窦房结功能障碍的阳性率亦分别进行组内比较。

1.5 统计学处理

所有指标采用SPSS19.0统计学软件进行数据分析。计量资料以 $\bar{x} \pm s$ 表示,计数资料以百分率表示;计量资料采用 t 检验,分类资料及率的比较采用 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

2 结 果

入选的358例房颤患者中,与非老年组比较,老年组中女性患者更多($P < 0.05$),合并高血压及器质性心脏病的比例更高(均 $P < 0.001$),心房脑钠肽(brain natriuretic peptide, BNP)水平亦明显升高($P < 0.001$;表1)。两组患者的房颤病史、左房内径及左室射血分数差异无统计学意义($P > 0.05$)。导管消融术前,共有36例(10.1%)患者检出房颤发作终止后长间歇,其中老年组26例,非老年组10例,两组患者比较,除年龄外基线资料差异均无统计学意义($P > 0.05$;表2)。

术前合并和不合并房颤发作终止后长间歇的患者比较,前者首次消融后的复发率显著高于后者(47.2% vs 29.8%, $P < 0.05$)。36例合并房颤发作终止后长间歇的患者中,老年和非老年患者术后的房颤复发率差异无统计学意义($P > 0.05$)。出院时,两组患者分别有21例(80.8%)和9例(90%)口服AAD,两组间差异无统计学意义($P > 0.05$)。

术前合并房颤终止后长间歇的10例非老年患者经射频消融术后,随访期间8例患者的窦房结功能恢复正常,仅有2例(20.0%)存在窦房结功能障碍,其中1例植入永久起搏器。然而,26例术前合并房颤终止后长间歇的老年患者在消融术后仍有17例(65.4%)出现窦房结功能障碍,其中6例植入永久起搏器治疗,6例因存在与窦性停搏、逸搏心律相关的症状亦有永久起搏器植入指征,余5例行动态心电图提示有 $> 3s$ 的RR长间歇,但无明显心动过缓相关的临床症状。综上所述,与非老年组比较,老年组患

者术前合并房颤终止后长间歇的比例(14.4% vs 5.6%, $P < 0.01$)与术后器质性窦房结功能障碍的阳性率(9.4% vs 1.1%, $P < 0.001$)均显著增高。与术前比较,非老年患者术后仍有窦房结功能障碍的比例显著降低(5.6% vs 1.1%, $P < 0.05$);而在老年患者中,术后窦房结功能障碍的阳性率较术前仅有降低趋势,差异无统计学意义(14.4% vs 9.4%, $P > 0.05$)。老年组术后窦房结功能的好转率显著低于非老年组(34.6% vs 80.0%, $P < 0.05$;表3)。

3 讨 论

本研究发现:(1)老年患者合并房颤发作终止后长间歇的比例显著高于非老年患者;(2)术前合并房颤发作终止后长间歇的患者消融术后房颤复发率较高;(3)与术前相比,非老年房颤患者射频消融术后窦房结功能明显改善,而老年患者多合并有器质性窦房结功能障碍,术后改善不明显,多数仍有植入永久起搏器的指征。

Inada等^[3]报道,37例术前合并房颤发作终止后长间歇的患者(平均年龄62岁)经多次导管消融治疗后,34例患者的房颤和窦性长间歇均被消除,仅有3例因窦房结功能进行性下降最终植入起搏器治疗。既往亦有研究证实房颤对窦房结功能的可逆性影响^[4],经起搏诱发犬房颤模型后可出现窦房结功能障碍,而房颤终止1周内窦房结功能恢复正常。Hadian等^[5]发现,对窦房结功能正常者快速起搏右心房10~15min后即可引起窦房结传导时间及恢复时间明显延长,表明短时间心房起搏即可使窦房结发生重构。快速房性心律失常引起窦房结重构的机制可能与直接下调窦房结细胞离子通道的表达、降低窦房结细胞的自律性有关^[6,7]。此外,房颤发作时,亦可导致窦房结细胞缺血及自主神经改变,从而影响窦房结的自律性。但是,前述研究均未探讨年龄对合并房颤发作终止后长间歇患者消融术后窦房结功能的影响。本研究结果显示,合并房颤发作终止后长间歇的非老年患者出现的窦房结功能障碍与房颤发作相关,多为功能性改变,消除房颤后多数患者的窦

表3 导管消融术前、后患者窦房结功能障碍的比较
Table 3 Prevalence rate of sinus node dysfunction before and after CA

Group	n	Patients with prolonged sinus pauses before CA	Patients with SND after CA	Patients with SNFR	Patients with AF recurrence after CA among positive ones	Patients with AAD after CA among positive ones
Non-older	177	10 (5.6)**	2 (1.1)***#	8 (80.0)*	4 (40.0)	9 (90.0)
Older	181	26 (14.4)	17 (9.4)	9 (34.6)	13 (50.0)	21 (80.8)

CA: catheter ablation; SND: sinus node dysfunction; SNFR: sinus node functional restoration; AAD: antiarrhythmic drugs; NA: there is no significant difference. Positive ones were patients with prolonged sinus pauses before CA. Compared with older group, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; compared with patients with prolonged sinus pauses before CA, # $P < 0.05$

房结功能即可恢复正常。然而,合并房颤发作终止后长间歇的老年患者不同,行射频消融治疗后窦房结功能改善不明显,提示老年患者可能合并潜在的器质性窦房结病变。老年人的窦房结病变可能与增龄本身所致的心房肌纤维化及器质性心脏病相关。

本研究针对合并房颤发作终止后长间歇的不同年龄患者,比较了年龄对阵发性房颤终止后长间歇患者窦房结功能的影响,初步分析了房颤与窦房结功能障碍的关系。本研究提示,非老年患者阵发性房颤发作后的长间歇多继发于房颤本身,治疗的关键在于消除房颤,可首选导管消融术,因术后多数患者的窦房结功能可显著改善,无需植入起搏器。而合并房颤发作终止后长间歇的老年患者多存在潜在的窦房结病变,即使消除房颤后,多数患者仍可能会出现窦房结功能的进行性减退,须密切随访,必要时植入永久起搏器治疗。

【参考文献】

- [1] Hocini M, Sanders P, Deisenhofer I, *et al.* Reverse remodeling of sinus node function after catheter ablation of atrial fibrillation in patients with prolonged sinus pauses[J]. *Circulation*, 2003, 108(10): 1172–1175.
- [2] Khaykin Y, Marrouche NF, Martin DO, *et al.* Pulmonary vein isolation for atrial fibrillation in patients with symptomatic sinus bradycardia or pauses[J]. *J Cardiovasc Electrophysiol*, 2004, 15(7): 784–789.
- [3] Inada K, Yamane T, Tokutake KI, *et al.* The role of successful catheter ablation in patients with paroxysmal atrial fibrillation and prolonged sinus pauses: outcome during a 5-year follow-up[J]. *Europace*, 2013. [Epub ahead of print].
- [4] Elvan A, Wylie K, Zipes DP. Pacing-induced chronic atrial fibrillation impairs sinus node function in dogs. Electrophysiological remodeling[J]. *Circulation*, 1996, 94(11): 2953–2960.
- [5] Hadian D, Zipes DP, Olgin JE, *et al.* Short-term rapid atrial pacing produces electrical remodeling of sinus node function in humans[J]. *J Cardiovasc Electrophysiol*, 2002, 13(6): 584–586.
- [6] Chang HY, Lin YJ, Lo LW, *et al.* Sinus node dysfunction in atrial fibrillation patients: the evidence of regional atrial substrate remodelling [J]. *Europace*, 2013, 15(2): 205–211.
- [7] Yeh YH, Burstein B, Qi XY, *et al.* Funny current downregulation and sinus node dysfunction associated with atrial tachyarrhythmia: a molecular basis for tachycardia-bradycardia syndrome[J]. *Circulation*, 2009, 119(12): 1576–1585.

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