·临床研究·

导管射频消融治疗高龄心房颤动患者的临床评价

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【摘 要】 **目的** 评价高龄心房颤动(AF)患者接受导管射频消融治疗的有效性和安全性。**方法** 纳入 2008 年 1 月至 2014 年 8月在大连医科大学附属第一医院行房颤射频消融(RA)的 877 例患者,按年龄分为老年组(≥75 岁)68 例、年轻老年组(65~74 岁)320 例及对照组(<65 岁)489 例。记录 3 组患者的临床资料,分析对比 3 组患者术中并发症、手术时间、X 线曝光时间,比较术后血栓栓塞率、再住院率、二次手术率、术后抗心律失常药物服用率以及术后缓慢心室率比例。消融成功的定义:术后心电图或动态心电图未再出现持续时间超过 30 s 的房颤。采用 SPSS 19.0 统计软件,根据数据类型分别采用 χ^2 检验、方差分析或 LSD 检验进行分析。应用 Kaplan-Meier 分析分别比较持续性 AF 和阵发性 AF 不同年龄患者的导管消融成功率。**结果** 消融过程及安全性评价:3 组患者术中并发症(5.9% *vs* 3.1% *vs* 2.9%)、手术时间[(196.65 ± 34.45) *vs* (196.03 ± 40.02) *vs* (194.36 ± 37.89) min]、X 射线曝光时间[(19.81 ± 6.73) *vs* (19.44 ± 6.45) *vs* (18.69 ± 6.00) min],差异均无统计学意义。疗效评价:3 组患者随访(21.45 ± 6.31)个月,其术后血栓栓塞率(4.4% *vs* 3.4% *vs* 2.5%)、再住院率(23.5% *vs* 22.2% *vs* 18.0%)及二次手术率(11.8% *vs* 12.8% *vs* 12.3%),差异无统计学意义。但是,老年组患者在术后长期使用抗心律失常药物的比例相对较低(13.2% *vs* 29.4% *vs* 20.0%,$P=0.001$),术后动态心电图出现缓慢心室率的比例较高(23.5% *vs* 15.6% *vs* 12.3%,$P=0.033$)。Kaplan-Meier 生存分析结果显示持续性 AF 和阵发性 AF 不同年龄患者的导管消融成功率差异无统计学意义。**结论** 老年心房颤动患者的导管消融成功率和安全性与年轻患者相似。

【关键词】 心房颤动;老年人;导管消融
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Clinical evaluation of radiofrequency catheter ablation in treatment of atrial fibrillation in the elderly

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【**Abstract**】 **Objective** To investigate the efficacy and safety of radiofrequency catheter ablation in the very old patients of atrial fibrillation (AF). **Methods** A total of 877 AF patients who underwent catheter ablation in our hospital from January 2008 to August 2014 were recruited in this study. According to their age, they were divided into very old group (≥75 years old, $n=68$), aged group (65 – 74 years old, $n=320$) and control group (<65 years old, $n=489$). The clinical data were collected and analyzed. The incidence of intra-operative complications, operation time, X-ray exposure time, post-operative thromboembolic rate, readmission rate, reoperation rate, post-operative administration rate of antiarrhythmia drugs and slow heart rate were compared among the groups. Successful ablation was defined as having no >30 s AF in any 24-hour holter monitoring during the follow-up period. SPSS statistics 19.0 was used to perform the statistical analysis. Chi-square test, analysis of variance, or LSD test was employed for different data types. Kaplan-Meier survival analysis was adopted to compare the success rate of ablation between the persistent AF and paroxysmal AF patients at different ages. **Results** In the evaluation of ablation procedure and safety, there were no significant differences in the incidence rates of complications (5.9% *vs* 3.1% *vs* 2.9%), operation time[(196.65 ± 34.45) *vs* (196.03 ± 40.02) *vs* (194.36 ± 37.89) min] and X-ray exposure time[(19.81 ± 6.73) *vs* (19.44 ± 6.45) *vs* (18.69 ± 6.00) min] among the 3 groups. After a mean follow-up period of (21.45 ± 6.31) months, no obvious differences were found in the thromboembolism rate (4.4% *vs* 3.4% *vs* 2.5%), readmission rate (23.5% *vs* 22.2% *vs* 18.0%) and reoperation rate (11.8% *vs* 12.8% *vs* 12.3%) among the 3 groups. However, the very old group had lower rate of taking antiarrhythmic drugs (13.2% *vs* 29.4% *vs* 20.0%, $P=0.001$) and experienced higher rate

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of slow heart rate in holter monitoring (23.5% *vs* 15.6% *vs* 12.3%, $P = 0.033$) than the other 2 groups. Kaplan-Meiers survival analysis indicated that there was no difference in the success rate of ablation between the persistent AF and paroxysmal AF patients at different ages. **Conclusion** The success rate and safety of catheter ablation are similar between the old and young AF patients.

【Key words】 atrial fibrillation; aged; catheter ablation

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心房颤动(atrial fibrillation,AF)是临床上最常见的心律失常之一,脑卒中和心力衰竭是其主要并发症,可导致患者的生活质量严重下降,死亡率显著升高,疾病负担沉重[1,2]。随着年龄的增加,房颤发生率明显增高,≥65 岁及≥85 岁人群房颤发生率分别为 6% 和 10%[3],且更易发生"双向事件"(血栓及出血),导致预后更差[4]。导管射频消融(radio-frequency catheter ablation,RFCA)作为房颤的有效治疗手段现已被广泛接受,但该治疗在老年患者中的应用效果尚未完全明确[5]。考虑到安全性及疗效,高龄房颤患者的临床试验中多排除了 RFCA[6,7]。随着 RFCA 开展的日益广泛,越来越多的高龄 AF 患者接受了 RFCA 治疗[8]。本文旨在评价高龄 AF 患者接受 RFCA 治疗的有效性与安全性。

1 对象与方法

1.1 研究对象

入选 2008 年 1 月至 2014 年 8 月在大连医科大学附属第一医院行 RFCA 的 AF 患者 877 例,根据联合国世界卫生组织提出的新的年龄分段,将研究样本分为老年组≥75 岁(A 组)、年轻老年组 65 ~ 74 岁(B 组)及对照组 <65 岁(C 组)。

1.2 术前准备

所有患者术前均行 12 导联心电图(静息和发作时)、24 h 动态心电图、心脏彩超,同时行经食道超声检查排除左心房及左心耳血栓,行肺静脉 CT 及 CARTO 系统三维成像,了解肺静脉形态、开口及与左心房的关系。

1.3 方法

全身麻醉下,常规行双侧股静脉穿刺,置入冠状静脉窦电极导管和右室心尖部电极导管,做保护性起搏。穿刺 2 次房间隔,术中予肝素抗凝,监测并保持活化凝血时间(activated clotting time, ACT)≥300 s。经长鞘分别送入 Lasso 电极与消融导管。在 CARTO 三维标测系统指导下,构建肺静脉及左心房电解剖模型,通过 Lasso 电极记录患者肺静脉电位,采用 Cardio Lab 多导电生理仪记录体表心电图及腔内心电图。以冷盐水灌注导管进行消融,温度 43℃,功率 30 ~ 35 W。所有患者消融策略选择原则相同,即阵发性房颤(paroxysmal atrial fibrillation, PaAF)只进行环肺静脉隔离,持续性房颤(persistent atrial fibrillation, PeAF)在肺静脉隔离基础上进行碎裂电位和线性消融,如术中出现房扑则进行激动标测和相应的消融[9,10]。

1.4 术后用药

术后接受抗凝治疗至少 2 个月,如 CHA2DS2-VASc≥2 分,则长期抗凝。抗心律失常药物和胃黏膜保护剂至少应用 2 个月。

1.5 随访

所有患者术后均进行定期门诊随诊,在术后 1,3,6,12 和 24 个月接受 24 h 动态心电图检查,如有心悸、胸闷等症状,门诊或急诊记录心电图。消融成功的定义为术后心电图或动态心电图未再出现持续时间超过 30 s 的 AF。

1.6 统计学处理

采用 SPSS 19.0 软件分析数据。计数资料以百分率表示,组间比较采用 χ^2 检验;计量资料以均数 ± 标准差($\bar{x} \pm s$)表示,组间比较采用方差检验,两两比较 LSD 检验。应用 Kaplan-Meier 分析分别比较不同年龄 PaAF 和 PeAF 患者的导管消融成功率。$P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 三组患者基线资料比较

入组患者 877 例,其中 A 组 68 例、B 组 320 例、C 组 489 例。3 组患者除年龄外,其他基本临床资料差异无统计学意义(表 1)。

2.2 三组患者 RFCA 疗效的比较

三组患者术后随访(21.45 ± 6.31)个月,将纳入患者区分为 PaAF 和 PeAF,分别比较不同年龄段的消融成功率,结果显示差异均无统计学意义(图 1,图 2)。三组术后出现血栓栓塞、需再次住院及二次手术的患者差异亦均无统计学意义(表 2)。

2.3 三组患者 RFCA 安全性比较

三组患者的严重并发症(心包填塞、动静脉瘘和严重的皮下血肿等)差异无统计学意义。A、B、C 三组患者手术时间分别为(196.65 ± 34.45) min,(196.03 ± 40.02) min 以及(194.36 ± 37.89) min,

表1 三组基线资料比较

Table 1 Comparison of baseline characteristics among three groups

Item	≥75 years group (n=68)	65-74 years group (n=320)	<65 years group (n=489)	P value
Age(years, $\bar{x}\pm s$)	77.12±1.87	68.81±2.91	55.49±7.53	0.000
Male[n(%)]	40(58.8)	183(57.2)	252(51.5)	0.209
PaAF[n(%)]	50(73.5)	237(74.1)	335(68.5)	0.208
Hypertension[n(%)]	46(67.6)	166(51.9)	260(53.2)	0.055
Diabetes mellitus[n(%)]	14(20.6)	54(16.9)	78(16.0)	0.624
Coronary heart disease[n(%)]	9(13.2)	24(7.5)	37(7.6)	0.250
Stroke[n(%)]	13(19.1)	56(17.5)	68(13.9)	0.275
Heart failure[n(%)]	11(16.2)	30(9.4)	39(8.0)	0.087
Dilated cardiomyopathy[n(%)]	3(4.4)	9(2.8)	11(2.2)	0.559
Hypertrophic cardiomyopathy[n(%)]	2(2.9)	7(2.9)	14(2.9)	0.829
Valvular heart disease[n(%)]	5(7.4)	14(4.4)	20(4.1)	0.472
TSH(mIU/L, $\bar{x}\pm s$)	3.21±2.26	2.86±1.84	2.81±1.75	0.258
Hb(g/L, $\bar{x}\pm s$)	132.01±15.39	132.57±15.68	132.25±15.49	0.942
LDL-C(mmol/L, $\bar{x}\pm s$)	2.28±0.79	2.62±1.51	2.68±1.59	0.132
AF course(years, $\bar{x}\pm s$)	8.51±10.37	7.01±7.85	6.91±7.61	0.293
LVEF(%, $\bar{x}\pm s$)	57.70±2.30	57.98±3.58	58.20±3.54	0.448
Left atrial diameter(mm, $\bar{x}\pm s$)	38.06±4.13	38.17±4.11	37.73±4.50	0.343

PaAF: paroxysmal atrial fibrillation; TSH: thyroid stimulating hormone; Hb: hemoglobin; LDL-C: low-density lipoprotein cholesterol; AF: atrial fribrillation; LVEF: left ventricular ejection fraction

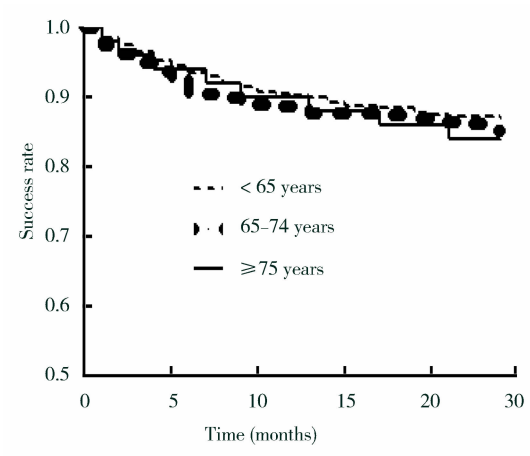


图1 三组患者中阵发性房颤的消融成功率的比较

Figure 1 Comparison of success rate of ablation in PaAF patients among three groups

PaAF: paroxysmal atrial fibrillation

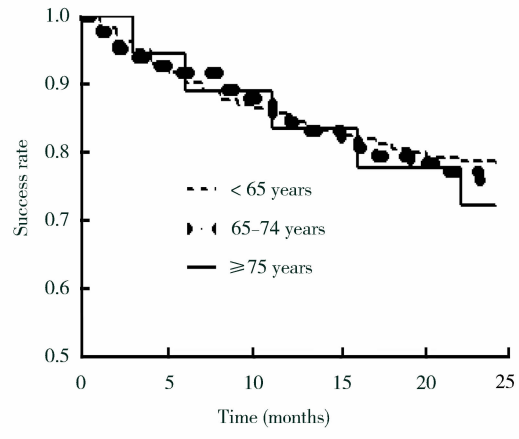


图2 三组患者中持续性房颤的消融成功率比较

Figure 2 Comparison of success rate of ablation in PeAF patients among three groups

PeAF: persistent atrial fibrillation

表2 三组患者手术后观察指标比较

Table 2 Comparison of post-operative data among three groups [n(%)]

Item	≥75 years group (n=68)	65-74 years group (n=320)	<65 years group (n=489)	P value
Complication	4(5.9)	10(3.1)	14(2.9)	0.412
Success	55(80.9)	265(82.8)	411(84.0)	0.764
Thromboembolism	3(4.4)	11(3.4)	12(2.5)	0.552
Second operation	8(11.8)	41(12.8)	60(12.3)	0.960
Rehospitalization	16(23.5)	71(22.2)	88(18.0)	0.257
Post-operative antiarrhythmia drugs	9(13.2)	94(29.4)	99(20.0)	0.001
Post-operative slow heart rate	16(23.5)	50(15.6)	60(12.3)	0.033

差异无统计学意义($P>0.05$)。三组患者术中X线曝光时间分别为(19.81±6.73) min,(19.44±6.45) min以及(18.69±6.00) min,差异无统计学意义($P>0.05$)。

术后随访资料显示,老年组患者术后存在更多的缓慢性心律失常,显著高于年轻老年组和对照组(23.5% *vs* 15.6% *vs* 12.3%,$P=0.033$)。同时,老年组患者长期口服抗心律失常药的比例也显著低于其他两组(13.2% *vs* 29.4% *vs* 20%,$P=0.001$,表2)。

3 讨 论

随着年龄的增加,AF的发生率也随之增加。临床上对于AF的治疗策略主要是抗心律失常药物(胺碘酮和普罗帕酮等)、抗凝治疗(华法林和新型抗凝药等)以及RFCA。高龄患者免疫和代谢等机体各方面功能均减弱,且普遍合并更多的基础性疾病,长期大量服用抗心律失常及抗凝药物发生不良反应的风险相对更高。Zaidenstein等[11]研究了住院患者服用心血管药物如胺碘酮、普罗帕酮以及抗凝药物华法林,发现发生不良反应的患者年龄更高且住院时间更长,其中45%的患者存在AF,不良反应主要包括服用华法林的患者出现了出血和皮肤坏死,服用β受体阻滞剂的患者出现了缓慢性心律失常和偏执狂反应,服用普罗帕酮的患者出现了室性心律失常等。可见高龄患者长期服用药物治疗AF相对于年轻患者的疗效差,且更容易发生严重的不良反应。此外,老年患者服用抗心律失常药物的依从性差,多数不能长期坚持。本研究还进一步发现,老年患者术后也合并更多的缓慢性心律失常,这可能与年龄老化、老年患者窦房结功能退化相关,导致患者对抗心律失常药物治疗的耐受性差。

年龄本身就是AF患者发生栓塞的危险因素之一,合并多种基础性疾病的高龄AF患者,往往也是栓塞和出血的高危患者[12]。虽然华法林预防高龄非瓣膜性AF患者血栓的效果并不比年轻患者差[13],但是高龄患者对华法林的依从性较差,且华法林对老年患者的安全性相比年轻患者差,尤其是严重出血的风险高[14,15]。通过导管消融恢复并维持窦律,使得部分患者可以停用抗凝治疗,从而极大提高老年患者的生活质量,并降低抗凝治疗导致的出血风险。

上述老年患者的临床特点均提示,老年患者通过RFCA长期维持窦律,其获得的治疗益处相对更多。RFCA已经成为转复并维持窦性心律的重要手段之一,其安全性与有效性也得到了验证。多项研究表明,RFCA治疗AF在维持窦律、改善生活质量、降低房颤复发率及减轻复发时症状等方面明显优于抗心律失常药物治疗。多中心、前瞻性的CACAF试验[16]比较了RFCA与药物治疗的有效性与安全性,1年随访结果显示,药物治疗组的复发率明显高于RFCA组,而RFCA组严重的并发症极低。RAAFT-2临床试验[17]也得出了相似的结论。由此可见,RFCA在治疗AF上具有显著疗效,并且有较高的安全性。Corrado等[7]对≥75岁行房颤RFCA的患者进行了(20±14)个月的随访,成功率高达73%。Zado等[18]比较了<65岁、65~74岁以及≥75岁房颤RFCA的患者,平均随访27个月后,其有效性无统计学差异。Bhargava等[19]报道了与年轻患者相似的成功率。本研究也得出了相似的结论,老年组、年轻老年组与对照组的成功率也与上述研究相似。此外,本研究还发现,老年患者在术后血栓栓塞、再住院及二次手术等指标上与年轻患者也不存在明显差异,表明在RFCA治疗心房颤动的疗效方面,并不存在年龄差异。

老年高龄AF患者往往合并多种基础性疾病,患者病情往往比年轻患者更加复杂,接受有创介入治疗的风险相对高于年轻患者。因此,老年患者RFCA治疗的安全性尤其需要重视。Lioni等[20]通过对比≥65岁及<65岁的AF患者RFCA中并发症出现的情况,发现RFCA的安全性与年龄无明显关系。本研究分析比较了出现的严重并发症,如心包填塞、严重皮下血肿、动静脉瘘等,结果表明老年组、年轻老年组与对照组严重并发症的比例差异无统计学意义。而且,老年组、年轻老年组与对照组的手术时间与X线曝光时间也不存在明显差异。

综上所述,RFCA同样适用于老年高龄的AF患者,手术的成功率和并发症发生率与年轻患者相近,能够显著改善老年AF患者的生活质量,同时能够显著降低大量服用抗心律失常及抗凝药物带来的不良反应。

本研究具有一定的局限性,即只是单中心的研究,且高龄患者较少,我们期待更多多中心、大样本的研究。

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