论著·公共卫生智库

累积身体圆度指数每增一档,绝经后心脏代谢性共病风险翻倍:基于CHARLS的队列研究与公共卫生筛查启示

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[摘要] **目的** 心脏代谢性共病(cardiometabolic multimorbidity,CMM)与严重健康结局相关;绝经是女性心血管疾病的独立危险因素,该阶段中心性肥胖风险增加;身体圆度指数(body roundness index,BRI)能有效反映内脏肥胖。探讨BRI的累积暴露水平与我国绝经后女性CMM风险的关联强度,以评估累积BRI(cumulative body roundness index,cuBRI)作为CMM长期风险标志物和简易筛查工具的潜力。**方法** 基于中国健康与养老追踪调查(China Health and Retirement Longitudinal Study,CHARLS)2011—2020年数据,纳入3 780名绝经后女性作为研究对象。采用多因素Logistic回归模型分析cuBRI、BRI动态轨迹与CMM风险的关联;利用限制性立方样条(restricted cubic splines,RCS)曲线检验剂量-反应关系;通过亚组分析考察效应修饰,并采用Bonferroni及错误发现率(false discovery rate,FDR)校正控制假阳性;使用ROC曲线比较cuBRI与BMI的预测能力。**结果** 完全调整模型显示,cuBRI每增加1个四分位间距(interquartile range,IQR),CMM风险增加112.4%(*OR*=2.124,95%*CI*:1.901~2.373,*P*<0.001);与cuBRI最低IQR组相比,最高IQR组的CMM风险显著升高(*OR*=4.701,95%*CI*:3.661~6.081,*P*<0.001)。逐步Logistic回归结果进一步证实,cuBRI、BMI、年龄、血脂异常、肾脏疾病、抑郁评分、C反应蛋白(C-reactive protein,CRP)是CMM的独立危险因素(均*P*<0.01);RCS曲线分析进一步显示,cuBRI与CMM风险呈线性正相关关系($P_{overall}$<0.001,$P_{nonlinear}$=0.224),当cuBRI>18.346时,CMM呈显著持续上升趋势。ROC曲线显示,cuBRI(AUC=0.742)预测CMM的能力与BMI(AUC=0.747)相当。亚组分析显示,经FDR校正和Bonferroni校正后,在年龄45~<60岁、年龄≥60岁、无血脂异常、无肾脏疾病、流调中心抑郁量表(center for epidemiologic studies depression scale,CES-D)评分<10分以及BMI为18.5~<24.0 kg/m^{2}的亚组中,cuBRI与CMM的正向关联仍保持稳健($P_{Bonferroni}$均<0.05)。**结论** cuBRI水平升高与我国绝经后女性CMM患病风险呈显著正向关联,其预测效能与BMI相当,提示其可能有助于反映长期中心性肥胖负荷,用于识别CMM高危人群。**对策** 依托"健康中国2030"及国家基本公共卫生服务框架,建议将cuBRI纳入绝经后女性基层随访内容,识别高危人群(cuBRI>18.346),实施生活方式干预及代谢指标综合管理;cuBRI与BMI联合应用或可优化风险分层,其因果效应及最优切点尚需干预性研究验证。

[关键词] 身体圆度指数;心脏代谢性共病;绝经后女性;中国健康与养老追踪调查
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Every one-grade increase in body roundness index doubles the risk of postmenopausal cardiometabolic multimorbidity: a CHARLS-based cohort study and its implications for public health screening

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[**Abstract**] Objective Cardiometabolic multimorbidity(CMM) is associated with severe health

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outcomes; menopause is an independent risk factor for cardiovascular disease in women, and the risk of central obesity is also increased during this phase. Body roundness index(BRI) can effectively reflect visceral obesity. This study aims to investigate the of strength association between cumulative exposure to BRI and CMM risk in postmenopausal Chinese women, and to evaluate the potential of cumulative(cuBRI) as a long-term risk marker and a simple screening tool for CMM. **Methods** Based on data from the China Health and Retirement Longitudinal Study(CHARLS) from 2011 to 2020, 3 780 postmenopausal women were enrolled as study participants. Multivariate logistic regression models were used to analyze the association of cuBRI and BRI trajectories with CMM risk; restricted cubic splines(RCS) curves were employed to examine the dose-response relationship; subgroup analyses were conducted to determine effect modification, and Bonferroni and false discovery rate(FDR) corrections were applied to control false positives. ROC curves were plotted to compare the predictive performance of cuBRI with that of BMI. **Results** The fully adjusted model showed that for every 1-interquartile range(IQR) increase in cuBRI, the risk of CMM increased by 112.4%(*OR*=2.124, 95%*CI*: 1.901 to 2.373, *P*<0.001); compared with the lowest cuBRI IQR group, the risk of CMM was significantly higher in the highest cuBRI IQR group(*OR*=4.701, 95%*CI*: 3.661 to 6.081, *P*<0.001). **Results** from stepwise logistic regression further confirmed that cuBRI, BMI, age, dyslipidemia, kidney disease, depression scores, and C-reactive protein(CRP) were independent risk factors for CMM(all *P*<0.01). RCS analysis further demonstrated a linear positive correlation between cuBRI and CMM risk($P_{overall}$<0.001, $P_{nonlinear}$=0.224). When cuBBI>18.346, CMM risk shows a significant and sustained upward trend. ROC curve analysis indicated that cuBRI(AUC=0.742) showed a predictive performance for CMM comparable to that of BMI(AUC=0.747). Subgroup analyses revealed that, after FDR and Bonferroni corrections, the positive association between cuBRI and CMM remained robust in the following subgroups: those aged 45 to <60 years, those aged ≥60 years, those without dyslipidemia, those without kidney disease, those with a score of center for epidemiologic studies depression scale(CES-D) <10, and BMI of 18.5 to <24.0 kg/m^2 (all $P_{Bonferroni}$<0.05). **Conclusion** Elevated cuBRI levels are significantly and positively associated with the risk of CMM in postmenopausal Chinese women, and their predictive performance is comparable to that of BMI, suggesting that it may help reflect long-term central obesity burden, and can be used to identify high-risk populations for CMM. **Countermeasures** Under the framework of "Healthy China 2030" initiative and the national framework for basic public health services, it is recommended that cuBRI be incorporated into primary-care follow-up protocols for postmenopausal women to identify high-risk populations(cuBRI >18.346), and to implement lifestyle interventions and comprehensive management of metabolic indicators. The combined application of cuBRI and BMI may optimize risk stratification, and its causal effects and optimal cutoff point require validation through intervention studies.

[**Key words**] body roundness index; cardiometabolic multimorbidity; postmenopausal women; China Health and Retirement Longitudinal Study

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心脏代谢性共病(cardiometabolic multimorbidity,CMM)是慢性共病的一种特定类型,指同一个体同时罹患2种或2种以上的心脏代谢性疾病[1]。通常包括2型糖尿病(type 2 diabetes mellitus,T2DM)、缺血性心脏病(ischemic heart disease,IHD)、中风,既往亦有研究将高血压和血脂异常等纳入共病范畴[2]。一项基于我国超过百万参与者的研究表明[3],女性CMM的发病率约为男性的1.5倍;在另一项针对我国4 832名女性的研究中,CMM的患病率从围绝经期的45~54岁时为28.5%,增长至75岁时的65.3%,且提示CMM与全因死亡呈正相关[4]。考虑到CMM及其组分疾病对中国的医疗卫生体系构成沉重的经济负担[5],因此识别其早期风险因素并实施有效干预显得尤为迫切。

一方面,绝经是女性心血管疾病的独立危险因素,其潜在机制可能与雌激素水平下降、糖脂代谢异常等因素有关[6-7]。绝经期是女性生命周期中的一个关键转折点,也为制定心血管疾病预防策略提供了重要机会窗口[8]。因此,针对此人群的研究至关重要。另一方面,肥胖和脂质代谢异常同样是驱动CMM发展的重要因素。肥胖与胰岛素抵抗(insulin resistance,IR)、血脂异常密切相关,这些因素共同驱动糖尿病、IHD等CMM组分的发展[9]。身体圆度指数(body roundness index,BRI)是一项旨在评估内脏肥胖程度的新指标[10],相较于传统的体质指数(body mass index,BMI),其优势在于结合了身高与腰围(waist circumference),能更精确地量化中心性肥胖。

然而,既往研究主要基于单时间点测量[11],仅探讨了BRI与其他传统人体测量指标如BMI、腰围、腰臀

比(waist-to-hip ratio,WHR)等在预测多种族亚洲人群的内脏脂肪分布和胰岛素敏感性方面的关系[12],或是探讨BRI联合其他指标与CMM的关系[13],均未关注到肥胖负荷的动态演化特征。由于绝经后人群的激素变化及CMM的发生发展是长期积累的过程,基于多时间点测量得出的累积指标和动态轨迹模式,或许能更好地捕捉代谢紊乱和慢性炎症的协同效应。为探究该问题,本研究旨在利用中国健康与养老追踪调查(China Health and Retirement Longitudinal Study,CHARLS)的大规模人群数据,系统评估BRI累积暴露和动态轨迹与我国中老年绝经后女性CMM发生风险之间的关系,以期为该人群的早期风险识别提供简便有效的评估工具。

1 资料与方法

1.1 数据来源与研究人群

本项队列研究采用了CHARLS数据集,该调查由北京大学国家发展研究院主持,是一项全国性前瞻性队列研究,涵盖了中国28个省份中年龄≥45岁的居民的数据。在2011年CHARLS全国基线研究中,采用按规模大小比例的概率抽样方法。全国范围内共招募了17 708名参与者,此后每隔2~3年对每位参与者进行随访(第2轮随访于2013年进行,第3轮于2015年,第4轮于2018年,第5轮于2020年)。该研究获北京大学生物医学伦理审查委员会批准(家庭调查:IRB00001052-11015;生物标志物:IRB00001052-11014)[14]。

本研究采用2011—2020年的CHARLS数据。纳入标准:2011年CHARLS数据库中收录的受试者。排除标准:①年龄<45岁的参与者;②未绝经的个体;③基线调查(2011年)时糖尿病或高血糖、心肌梗死、冠心病、心绞痛、或其他心脏问题、卒中、高血压等数据缺失的参与者;④结局数据(2020年)中糖尿病或高血糖、卒中数据缺失的参与者;⑤身高及腰围数据缺失的参与者;⑥基线调查(2011年)中已存在CMM的参与者。最终,共有3 780名参与者被纳入分析,详见图1。

1.2 绝经后女性的定义

通过问卷问题“您绝经了吗”以及“您是什么时候开始绝经的”进行判定。若记录了绝经的年份或年龄,则判定为已绝经。

1.3 CMM、BRI、cuBRI和BRI动态轨迹的定义

本研究的结局变量为CMM,暴露变量为2011—2015年间BRI值的变化。考虑到高血压与心血管疾病密切相关,且既往研究常将其纳入CMM范畴[2,15-16],为尽可能扩大符合标准的人群,本研究将高血压也纳入CMM定义。CMM的定义标准为:个体同时患有以下4种疾病中的至少2种。①T2DM符合以下任一条件:糖化血红蛋白(glycated hemoglobin, HbA1c)≥6.5%、空腹血糖(fasting blood glucose, FBG)≥7 mmol/L、自我报告确诊史(“您是否被医生诊断为糖尿病”)或使用降糖药物[17]。②心血管疾病的判定依据自我报告问题:“您是否被医生诊断为心脏病、冠状动脉疾病、心绞痛或其他心脏问题”。③脑卒中的判定依据自我报告问题:“您是否被医生诊断为脑卒中”。④高血压定义为:平均收缩压≥140 mmHg、平均舒张压≥90 mmHg、高血压病史(“您是否被医生诊断为高血压”)或使用降压药物。

BRI计算公式为:$BRI=364.2-365.5\times\left[1-\frac{(\text{腰围}/2\pi)^2}{(0.5\times\text{身高}\times100)^2}\right]^{\frac{1}{2}}$。累积身体圆度指数(cumulative body roundness index,cuBRI)采用线性模型计算,公式为:$cuBRI=[(BRI_{2011}+BRI_{2015})/2]\times4$,式中$BRI_{2011}$和$BRI_{2015}$分别为2011年(第1轮)和2015年(第3轮)测得的BRI[18]。

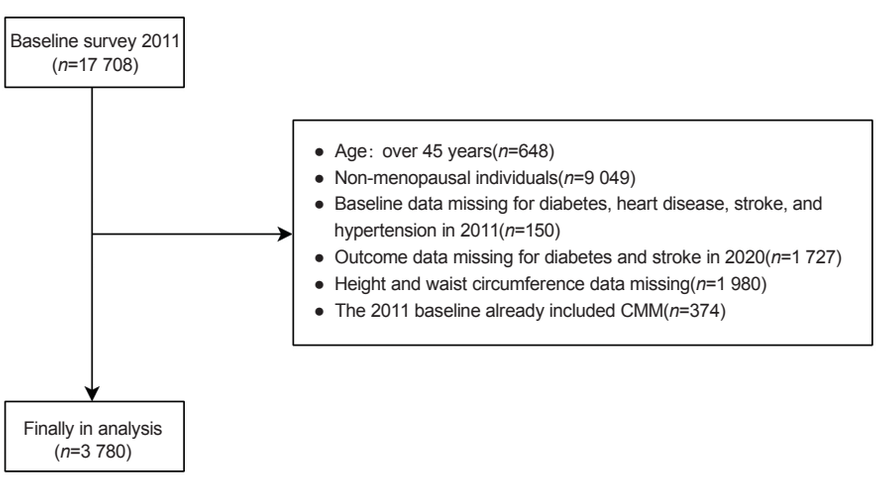


图1 研究对象筛选流程图

Figure 1 Flowchart for screening participants

研究使用了基于组的轨迹模型(group-based trajectory modeling,GBTM)来识别BRI的动态轨迹。通过提取每个个体的二次项系数(a)、一次项系数(b)和常数项(c),利用高斯混合模型进行概率聚类。依次测试了2类、3类和4类模型,参考了NAGIN[19]的基于组的轨迹建模意见及其他既往研究,通过以下综合标准评估最佳拟合模型的选择[20]:①贝叶斯信息准则值较低或随类别增加,下降趋于平缓的模型优先;②每个轨迹类别至少有5%的参与者;③平均后验概率>70%;④正确分类的几率(odds of correct classification,OCC)>5;⑤不同类别的轨迹曲线在视觉上具有明显且合理的区分度。通过GBTM聚类,本研究将轨迹分为3类:第1类低BRI稳定组(n=2 658)、第2类中BRI上升组(n=319)和第3类高BRI稳定组(n=803),见图2。

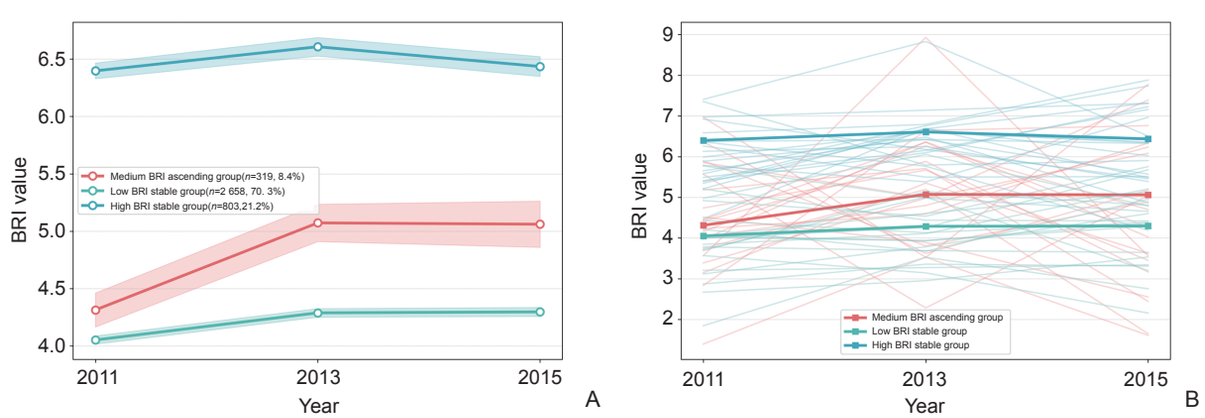
1.4 协变量的定义

CHARLS研究人员根据预先指定的标准收集变量,本研究基于临床角度考量并参考既往相关文献[21-22],从基线调查中收集了以下数据作为研究的协变量:年龄、婚姻、教育程度、居住地、吸烟、饮酒、血脂异常、肾脏疾病、是否购买保险、睡眠时间、流调中心抑郁量表(center for epidemiologic studies depression scale,CES-D)、C-反应蛋白(C-reactive protein,CRP)。

身高和腰围数据来源于体检记录。所有体格测量均由经过专业培训的移动健康筛查中心技术人员执行,并记录在案,以确保数据准确性。参与者在测量前被要求脱去衣物和鞋子。身高在站立时测量,腰围在站立时测量,位置在肋骨下缘与髋部上缘的中点。吸烟与饮酒情况通过受试者自我报告获取("您现在是否吸烟""您曾经是否饮酒")。血脂异常定义为:总胆固醇(total cholesterol,TC)≥240 mg/dL、低密度脂蛋白胆固醇(low density lipoprotein cholesterol,LDL-C)≥160 mg/dL、高密度脂蛋白胆固醇(high density lipoprotein cholesterol,HDL-C)<40 mg/dL、甘油三酯(triglyceride,TG)≥200 mg/dL、血脂异常病史("您是否被医生诊断为血脂异常")和/或使用降脂药物[23]。肾脏疾病定义为自我报告确诊("您是否曾被医生诊断为肾脏疾病")或使用相关药物[24]。CES-D评分沿用既往研究,将其视为二分类变量,≥10分表示有抑郁症状[25]。

1.5 统计学分析

统计分析使用R软件(版本4.5.1)进行。连续变量以$\bar{x}\pm s$或$M(P_{25},P_{75})$描述,组间比较采用t检验或Mann-Whitney U检验;分类变量以频数(%)描述,组间比较采用χ^2检验。采用多因素Logistic回归分析cuBRI、BRI四分位数及BRI轨迹与CMM风险的关联,共构建3个模型:模型1未调整协变量;模型2调整年龄、婚姻、教育程度、居住地、吸烟及饮酒;模型3为完全调整模型,在模型2基础上进一步调整血脂异常、肾脏疾病、医疗保险、睡眠时间、CES-D评分及CRP。将上述变量及cuBRI、BRI轨迹、BRI四分位数、BMI纳入多因素逐步Logistic回归(向后法)并基于赤池信息准则(Akaike information criterion,AIC)进行评估,进而筛选CMM独立危险因素。通过反复剔除对模型拟合贡献最小的变量,最终保留AIC值最小的模型,从而得到CMM的独立危险因素集合,并以方差膨胀因子(variance inflation factor,VIF)评估共线性;采用限制性立方样条(restricted cubic splines,RCS)曲线分析cuBRI与CMM的剂量-反应关系,通过ROC曲线比较cuBRI与BMI的预测效能。亚组分析中采用Bonferroni法及错误发现率(false discovery rate,FDR)进行多重比较校正。变量缺失率均<30%,采用R软件Mice包进行5次多重插补(预测均值匹配法),随机种子设为1、2、3、4以保证结果可重现。P<0.05表示差异具有统计学意义。



A: Three clusters identified by group-based trajectory modeling(GBTM); B: Trends in BRI from 2011 to 2015

图2 2011~2015年BRI变化的聚类分析

Figure 2 Cluster analysis of changes in body roundness index(BRI) in the postmenopausal Chinese women from 2011 to 2015

2 结果

2.1 按是否发生CMM划分的绝经后女性基线特征

本研究共纳入3 780名符合条件的绝经后受试者,其中有850(22.49%)人被诊断为CMM;教育水平为中学及以上的受试者占比39.31%;血脂异常的受试者共有288(7.62%)人;基线BRI的中位数为4.43(3.57,5.46)。CMM组和非CMM组在年龄、是否发生血脂异常、是否发生肾脏疾病、是否发生高血压、是否发生糖尿病、是否发生心脏病、是否发生卒中、腰围、睡眠时间、BMI、TC、TG、HDL-C、LDL-C、CRP、CES-D评分、BRI_{2011}、BRI_{2013}、BRI_{2015}等方面差异存在统计学意义($P<0.05$),见表1。

2.2 cuBRI四分位分组人群的基线特征

根据cuBRI的IQR分为4组,随着个体cuBRI水平的升高,新发CMM的发生率呈现持续上升趋势,分别为10.48%、17.57%、24.34%和37.57%,差异具有统计学意义($P<0.01$),见表2。

2.3 cuBRI升高与CMM风险增加显著相关

通过Logistic回归可发现cuBRI与CMM的患病率

表1 研究对象的基线特征表[例(%),$\bar{x}\pm s$,$M(P_{25},P_{75})$]

Table 1 Baseline characteristics of the participants with and without cardiometabolic multimorbidity(CMM) [$n(\%)$, $\bar{x}\pm s$, $M(P_{25},P_{75})$]

Variables	Total(n=3 780)	Non-CMM(n=2 930)	CMM(n=850)	P
Age/years	57(50, 63)	56(49, 62)	59(54, 65)	<0.001
Marital status				0.096
Other	452(11.96)	336(11.47)	116(13.65)	
Married/Cohabiting	3 328(88.04)	2 594(88.53)	734(86.35)	
Education				0.405
Below elementary school level	2 294(60.69)	1 763(60.17)	531(62.47)	
Elementary school	674(17.83)	520(17.75)	154(18.12)	
Middle school	587(15.53)	466(15.90)	121(14.24)	
College completed or above	225(5.95)	181(6.18)	44(5.18)	
Location				0.741
Town	1 212(32.06)	935(31.91)	277(32.59)	
Rural	2 568(67.94)	1 995(68.09)	573(67.41)	
Drink	541(14.31)	407(13.89)	134(15.76)	0.188
Smoke	212(5.61)	162(5.53)	50(5.88)	0.757
Dyslipidemia	288(7.62)	177(6.04)	111(13.06)	<0.001
Kidney	174(4.60)	119(4.06)	55(6.47)	0.004
Insurance	3 598(95.19)	2 788(95.15)	810(95.29)	0.938
Height/m	1.53(1.49, 1.57)	1.53(1.49, 1.57)	1.53(1.49, 1.57)	0.535
Waist circumference/cm	85.00(78.00, 92.00)	83.50(77.00, 90.00)	89.60(83.00, 96.00)	<0.001
Sleep time/h	6.00(5.00, 8.00)	6.00(5.00, 8.00)	6.00(5.00, 8.00)	0.008
TC/(mg/dL)	194.85(170.88, 219.20)	193.69(170.49, 216.88)	199.10(175.23, 225.00)	<0.001
TG/(mg/dL)	110.62(78.76, 163.73)	107.08(77, 156.65)	129.21(88.50, 185.63)	<0.001
HDL-C/(mg/dL)	50.26(40.98, 59.92)	51.03(42.14, 61.08)	47.55(38.66, 56.73)	<0.001
LDL-C/(mg/dL)	117.53(95.88, 140.43)	116.75(95.1, 139.18)	120.04(99.74, 145.36)	<0.001
CRP/(mg/dL)	0.91(0.51, 1.87)	0.81(0.48, 1.66)	1.25(0.68, 2.77)	<0.001
CES-D	8(4, 13)	8(4, 13)	9(5, 14.75)	<0.001
BRI_{2011}	4.43(3.57, 5.46)	4.24(3.45, 5.24)	5.12(4.16, 6.09)	<0.001
BRI_{2013}	4.77(3.82, 5.71)	4.59(3.69, 5.52)	5.31(4.41, 6.35)	<0.001
BRI_{2015}	4.70(3.79, 5.73)	4.55(3.67, 5.47)	5.40(4.34, 6.41)	<0.001
cuBRI	18.27(14.92, 22.10)	17.58(14.42, 21.11)	20.89(17.15, 24.77)	<0.001

表2 根据cuBRI的IQR分组的CMM分布特征[例(%),$M(P_{25},P_{75})$]

Table 2 Distribution characteristics of CMM based on cuBRI quartile grouping [$n(\%)$, $M(P_{25},P_{75})$]

Variables	Total(n=3 780)	Q1(n=945)	Q2(n=945)	Q3(n=945)	Q4(n=945)	P
cuBRI	18.27(14.92, 22.10)	12.88(11.41, 13.99)	16.62(15.86, 17.45)	20.04(19.14, 20.96)	25.00(23.4, 27.32)	<0.001
CMM						<0.001
No	2 930(77.51)	846(89.52)	779(82.43)	715(75.66)	590(62.43)	
Yes	850(22.49)	99(10.48)	166(17.57)	230(24.34)	355(37.57)	

表3 cuBRI与CMM风险之间呈正向关联

Table 3 Positive correlation between cuBRI and CMM risk

Groups	Model 1		Model 2		Model 3	
	OR(95%*CI*)	*P*	*OR*(95%*CI*)	*P*	*OR*(95%*CI*)	*P*
cuBRI	2.255(2.026—2.509)	<0.001	2.182(1.957—2.432)	<0.001	2.124(1.901—2.373)	<0.001
Quartiles of cuBRI						
Q1	Reference		Reference		Reference	
Q2	1.821(1.397—2.385)	<0.001	1.841(1.410—2.415)	<0.001	1.837(1.402—2.416)	<0.001
Q3	2.749(2.135—3.562)	<0.001	2.680(2.078—3.479)	<0.001	2.584(1.996—3.366)	<0.001
Q4	5.142(4.034—6.605)	<0.001	4.922(3.850—6.340)	<0.001	4.701(3.661—6.081)	<0.001
P	<0.001		<0.001		<0.001	

表4 不同BRI轨迹类别与CMM风险之间的关联

Table 4 The relationship between different BRI trajectory categories and CMM risk

Groups	Model 1		Model 2		Model 3	
	OR(95%*CI*)	*P*	*OR*(95%*CI*)	*P*	*OR*(95%*CI*)	*P*
Low BRI stable	Reference		Reference		Reference	
Medium BRI ascending	0.689(0.525—0.912)	0.008	0.726(0.551—0.964)	0.024	0.739(0.560—0.984)	0.035
High BRI stable	1.938(1.449—2.613)	<0.001	1.910(1.425—2.582)	<0.001	1.854(1.376—2.519)	<0.001
P	<0.001		<0.001		<0.001	

之间存在正向关联。这种正向关联在模型3中保持一致(*OR*=2.124,95%*CI*:1.901~2.373,*P*<0.001),表明cuBRI每增加一个IQR,CMM的风险就会增加112.4%。此外,本研究将cuBRI由连续变量转换为分类变量并按IQR分组。在模型3中,与cuBRI的Q1组相比,Q2、Q3和Q4组与新发CMM的风险呈较高相关性;并且可以观察到,随着BRI水平的升高,新发CMM的风险逐渐增高,最强的正相关关联出现在Q4组(表3)。与低BRI稳定组相比,中BRI上升组发生CMM的风险显著降低(*OR*=0.739,95%*CI*:0.560~0.984,*P*=0.035),而高BRI稳定组发生CMM的风险显著升高(*OR*=1.854,95%*CI*:1.376~2.519,*P*<0.001),经多因素调整后结果仍具有统计学意义(表4)。cuBRI是CMM的独立危险因素,每增加一个IQR,CMM发生风险增加48.4%(*OR*=1.484,95%*CI*:1.248~1.764,*P*<0.001,表5)。其他保留的独立危险因素包括:BMI、年龄、血脂异常、肾脏疾病、抑郁评分、CRP。模型拟合优度:AIC=3 669.2,残差偏差较零模型显著下降。VIF评估最终模型的共线性,结果显示所有变量VIF<5,表明模型不存在严重共线性问题。

表5 经多因素逐步Logistic回归分析后保留的CMM相关危险因素

Table 5 CMM-related risk factors retained after stepwise logistic regression analysis

Variable	*β*	*SE*	*Z*	*OR*(95%*CI*)	*P*
Age	0.036	0.005	6.878	1.603(1.401—1.833)	<0.001
Dyslipidemia	0.607	0.137	4.438	1.835(1.403—2.399)	<0.001
Kidney	0.484	0.181	2.675	1.622(1.138—2.312)	0.007
CES-D	0.033	0.006	5.277	1.346(1.205—1.503)	<0.001
CRP	0.039	0.009	4.444	1.055(1.030—1.080)	<0.001
cuBRI	0.055	0.012	4.477	1.484(1.248—1.764)	<0.001
BMI	0.088	0.017	5.181	1.539(1.307—1.812)	<0.001

2.4 cuBRI与CMM风险之间呈线性正相关

本研究采用RCS曲线分析了cuBRI与CMM风险之间的剂量反应关系。如图3所示,cuBRI与CMM发生风险总体上呈线性正相关关系($P_{overall}$<0.001,$P_{nonlinear}$=0.224)。当cuBRI>18.346时,OR及其95%*CI*均明确>1,且随cuBRI增高,CMM发病风险呈持续性上升趋势。

2.5 cuBRI与BMI对CMM的预测效能相当

ROC曲线结果显示(图4),cuBRI的尤登指数为35.4%,AUC值为0.742(95%*CI*:0.708~0.775),敏感性

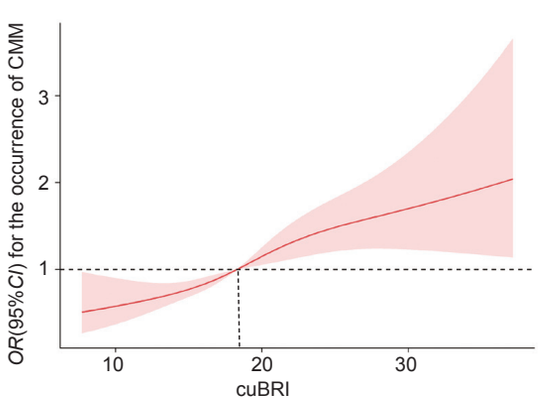


图3 RCS曲线显示cuBRI与CMM风险呈线性正相关

Figure 3 ROC curve analysis indicates a linear positive correlation between cuBRI and CMM outcomes

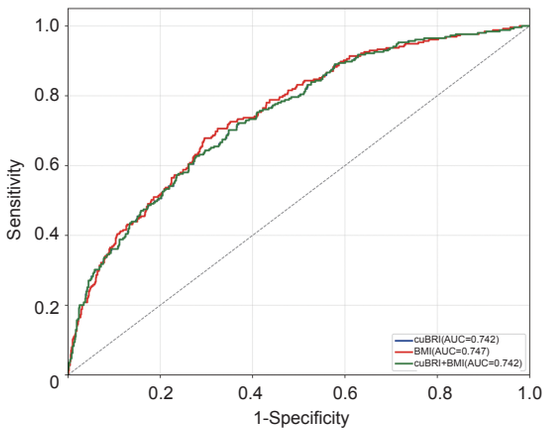


图4 cuBRI预测我国中老年绝经后女性发生CMM的ROC曲线

Figure 4 ROC curve of cuBRI for predicting CMM in postmenopausal women in China

70.2%,特异性65.2%;BMI的尤登指数为38.3%,AUC值为0.747(95%*CI*:0.713~0.781),其敏感性为67.8%,特异性为70.4%。cuBRI的预测性能与BMI相当。

2.6 经多重较正后,多个亚组中cuBRI与CMM的正向关联仍显著

亚组分析结果显示,cuBRI与CMM风险的正向关联在所有15个预设亚组中共有10个达到统计学显著性(*P*<0.05,图5)。经FDR校正和Bonferroni校正后,仍有6个亚组保持显著,分别是年龄45~<60岁(*OR*=1.696,95%*CI*:1.345~2.137)、年龄≥60岁(*OR*=1.473,95%*CI*:1.172~1.851)、无血脂异常(*OR*=1.502,95%*CI*:1.257~1.795)、无肾脏疾病(*OR*=1.482,95%*CI*:1.246~1.762)、CES-D评分<10分(*OR*=1.606,95%*CI*:1.388~1.858)以及BMI为18.5~<24.0 kg/m^2(*OR*=1.506,95%*CI*:1.284~1.767),见表6;同时,研究发现各亚组交互作用不显著,表示暴露的效应在不同水平间无显著差异,整体结论一致,各分层变量与BRI轨迹的交互作用差异无统计学意义,见图6。

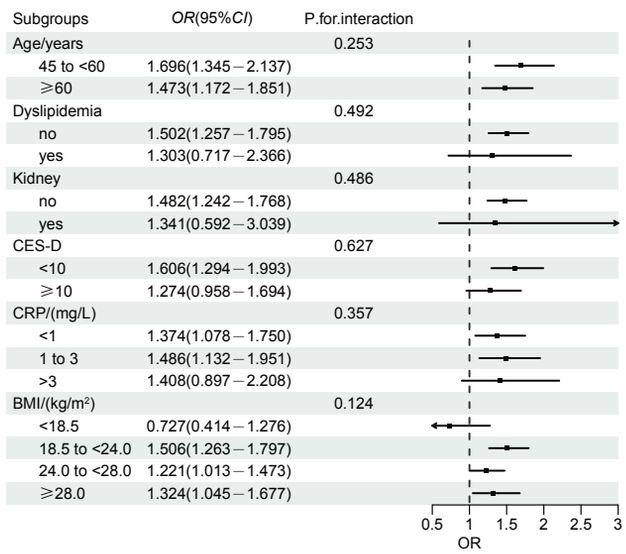


图5 cuBRI与CMM风险之间关联的亚组分析

Figure 5 Subgroup analysis of the association between cuBRI and CMM risk

表6 cuBRI与CMM风险关联经Bonferroni和FDR校正的亚组分析

Table 6 Subgroup analyses of the association between cuBRI and CMM risk after Bonferroni and false discovery rate(FDR) corrections

Subgroups	*OR*	$P_{Original}$	$P_{Bonferroni}$	P_{FDR}
Age/years				
45 to <60	1.696	<0.001	<0.001	0.000
≥60	1.473	0.001	0.015	0.003
Non-dyslipidemia	1.502	<0.001	<0.001	0.000
Non-kidney disease	1.482	<0.001	<0.001	0.000
CES-D<10	1.606	<0.001	<0.001	0.000
CRP/(mg/L)				
<1	1.374	0.010	0.150	0.019
1 to 3	1.486	0.004	0.060	0.009
BMI/(kg/m^2)				
18.5 to <24.0	1.506	<0.001	<0.001	0.000
≥28.0	1.324	0.020	0.300	0.033

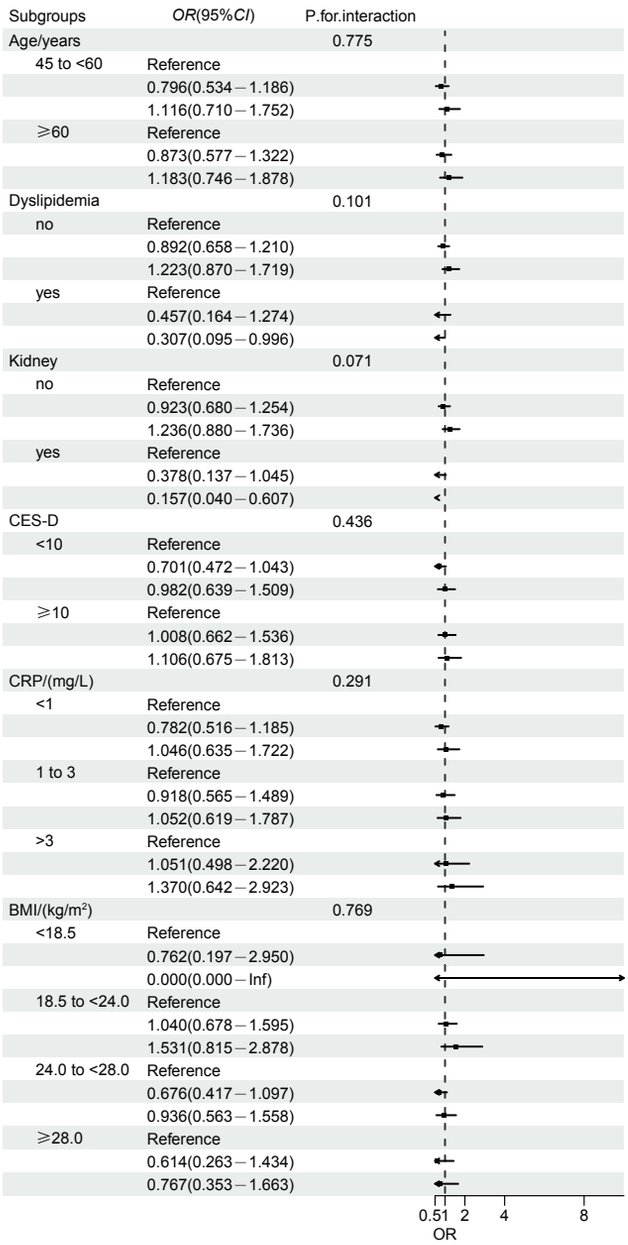


图6 BRI不同轨迹与CMM风险关联的亚组:未发现显著关联

Figure 6 No significant association is observed in the relationship between different BRI trajectories and CMM risk

3 讨论

本研究是首个在我国绝经后女性中探讨BRI累积暴露和动态轨迹与CMM关联的前瞻性分析。结果显示,在≥45岁的我国绝经后女性中,cuBRI水平升高与CMM发生风险呈显著正相关,且呈线性剂量-反应关系($P_{overall}$<0.001,$P_{nonlinear}$=0.224)。具体而言,cuBRI每增加1个IQR,CMM风险增加112.4%(*OR*=2.124,95%*CI*:1.901~2.373);与最低四分位组相比,最高四分位组CMM风险升高约3.7倍(*OR*=4.701,95%*CI*:3.661~6.081)。限制性立方样条曲线进一步提示,当cuBRI<18.346时,CMM风险处于较低水平,超过该值后风险显著上升。亚组分析经Bonferroni多重比较校正后显示,在年龄45~<60岁、年龄≥60岁、无血脂异常、无肾脏疾病、CES-D评分<10分以及BMI为18.5~<24.0 kg/m²的亚组中,cuBRI与CMM的正向关联依然稳健,这表明该关联具有较好的人群稳健性。逐步回归分析在最终模型中保留了cuBRI而非BRI动态轨迹,提示前者所反映的长期中心性肥胖累积负荷,可能较之短期轨迹变化或单次横断面测量,对识别绝经后女性CMM高危个体具有更重要的价值。

3.1 中国CMM疾病负担沉重,中心性肥胖通过IR与慢性炎症共同驱动绝经后女性发病

在当前我国心血管代谢疾病负担持续加重的背景下,深入理解CMM的发病机制并进行早期识别和筛查显得尤为重要。现阶段,我国T2DM、冠心病、卒中等心血管代谢性疾病的患病率、死亡率与经济负担持续攀升。一项GBD的报告指出,按全年龄残疾调整寿命年(disability-adjusted life-years,DALYs)计算,导致我国疾病负担最严重的两大病因仍是卒中和IHD[26]。另一项研究指出,2020—2030年间,仅我国糖尿病所占GDP的总成本比例将从1.58%上升至1.69%,糖尿病经济负担的增长速度快于我国经济增长[5]。

在机制上,CMM作为多种代谢异常共存的疾病,其发生发展与IR及慢性低度炎症密切相关。既往一项针对C反应蛋白-甘油三酯-葡萄糖指数(C-reactive protein-triglyceride-glucose index,CTI)的研究也证实了这一点[27]。中心性肥胖同样是公认的CMM危险因素[28],与皮下脂肪相比,内脏脂肪具有更强的代谢活性,其通过释放游离脂肪酸及促炎细胞因子,诱发IR与慢性低度炎症,从而损害血管功能并加速动脉粥样硬化[29-30];IR本身又可进一步激活炎症通路[31],形成恶性循环。这一病理生理基础支持了多种腹部肥胖指标与CVD的关联[32],最终逐渐发展成CMM。绝经后女性因激素变化存在独特的内脏脂肪累积倾向[33],使得BRI对该人群的代谢风险更为敏感。此外,在绝经后女性中需要关注共病的影响。肥胖与抑郁常共存并相互影响[34],共享下丘脑-垂体-肾上腺轴(hypothalamic-pituitary-adrenal axis,HPA)[35],且抑郁本身可增强炎症[36]并诱发IR[37],从而形成恶性循环,协同影响CMM的发生发展。

3.2 cuBRI与BMI预测效能相当,但反映长期内脏脂肪累积更具独特优势

cuBRI与BMI均为CMM的独立危险因素,经VIF评估,2者同时纳入模型未导致共线性问题,提示2者在预测CMM风险时具有互补作用。尽管cuBRI(AUC=0.742)的预测效能与BMI(AUC=0.747)相当,但BRI作为一个通过身高与腰围即可测算的简易指标,其优势在于能够反映长期内脏脂肪累积这一CMM的重要驱动因素。与之相对,BMI无法区分脂肪分布,ZHOU等[38]的研究也提及了这一点。BRI所代表的内脏脂肪可能主要通过"脂质代谢紊乱"和"慢性炎症"这2大通路促进CMM;一方面,内脏脂肪通过引发的IR可激活SREBP-1c通路促进胆固醇的合成[39];另一方面,内脏脂肪脂解作用增强,增加极低密度脂蛋白(very low-density lipoprotein,VLDL)的合成与分泌,最终导致LDL-C水平升高或质量改变而阻碍LDL-C的代谢和清除[40],从而加剧动脉粥样硬化进程[41]。因此,cuBRI所体现的长期脂肪分布异常累积暴露,对于风险评估具有独特的病理生理学意义。

3.3 cuBRI>18.346提示风险显著上升,且亚组关联保持稳健

一项基于CHARLS队列的研究提示BRI与心血管疾病之间存在非线性关联,BRI>3.61时,它与中老年人糖尿病人群心血管疾病风险呈正相关[13];另一项基于NHANES的横断面研究也显示[38],BRI与全因死亡率及心血管死亡率之间呈U型关系;这与本研究的限制性立方样条结果相似,当cuBRI>18.346时,CMM风险显著升高;这些结果共同提示,BRI的累积暴露与CMM风险存在稳健的正向关联。经过严格的多重比较校正后,亚组分析显示,在绝经后女性中,cuBRI与CMM风险的关联在≥45岁的整个中老年年龄段中均保持稳健。此外,在无血脂异常、无肾脏疾病、CES-D评分<10分以及BMI为18.5~24.0 kg/m^{2}的人群中,该关联同样通过了最严格的Bonferroni校正,提示cuBRI作为早期体脂分布指标,在尚未出现明显代谢紊乱或体质量异常的中老年人群中可能具有更纯粹的预警价值。所有交互作用P值均不显著,表明cuBRI的效应在不同亚组水平间无显著差异,整体结论一致。

3.4 优势与局限性

本研究的优势在于:①这是首个在我国绝经后女性这一特定高危人群中系统探讨BRI的累积暴露与动态轨迹与CMM关联的研究;②基于大规模全国性代表性样本,使结果具有良好的外推性。cuBRI作为一种安全、非侵入性且易于实施的指标,在资源有限的环境中具有推广潜力[12]。本研究也存在若干局限性:①CMM的诊断部分基于自我报告,可能存在信息偏倚,尤其是对心脏病和中风的诊断;②尽管已调整多种混杂因素,但存在残留混杂如未纳入分析的体力活动的可能性无法完全排除;③本研究为队列设计,cuBRI的因果效应及最优切点尚需外部验证或前瞻性干预研究证实;④部分研究对象在基线调查时处于围绝经期,该人群的激素水平波动可能夸大cuBRI与CMM风险的关联;⑤本研究未报告随访期间的失访率及失访原因,若失访与暴露或结局相关,可能导致估计偏倚。未来可通过孟德尔随机化、干预试验或更频繁的测量数据,进一步验证BRI及其累积暴露对CMM的因果效应及机制通路,并开展失访分析以评估其对结果稳健性的影响,为纳入临床指南提供更高级别证据。

3.5 对公共卫生实践的启示

在"健康中国2030"战略及国家基本公共卫生服务框架下,心血管代谢性疾病管理已纳入基层常态化工作。cuBRI仅需身高与腰围2项简易指标即可计算,操作成本低廉,适宜在基层医疗机构推广。建议依托现有老年人健康体检项目,将cuBRI纳入绝经后女性随访内容,以cuBRI>18.346作为高危人群识别参考切点,实现CMM风险的早期筛查与分层管理。对于cuBRI升高者,应优先实施生活方式干预,控制腰围增长、优化膳食结构,并将血糖、血脂、血压等代谢指标纳入综合管理;同时需加强针对绝经后人群的健康教育,提升其对中心性肥胖及共病协同危害的认知。cuBRI与BMI均为CMM独立危险因素且预测效能相当,但cuBRI在反映长期内脏脂肪累积方面具有独特优势,尤其在BMI正常但体脂分布异常的亚组中显示出更纯粹的预警价值,提示两者联合应用或可优化风险分层精度。

利益冲突 本文所有作者声明不存在利益冲突

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