·临床病例讨论·

Clinicopathological Conference

An octogenarian with chest pain, ST segment elevation and hypotension

(The fifth case)

Case Presentation

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An 81-year-old man was admitted to the hospital due to chest pain for 2.5 hours. Crushing or squeezing chest pain occurred after he had got upset 2.5 hours ago, and it was persistent, without radiation, concomitant with chest distress, palpitation, sweating, nausea, and with vomiting once. The symptoms could not be relieved by oral medication of anti-anginal Chinese herb pills (Su Xiao Jiu Xin Wan). After the onset of symptoms, the patient had no urination. Past history: exertional precordial pain attacks in recent 1 year, chronic bronchitis for 2 years and cigarette smoking for 60 years (10-20 sticks per day). He denied history of hypertension and diabetes. Physical examination: Bp 62/45mmHg, normal consciousness, painful complexion, automatic posture, warm extremities, no engorgement of both jugular veins, coarse respiratory sound and a few dry rales in both lung fields, heart border in normal range, heart rate 75 bpm with irregular rhythm, and premature beats could be heard at about 10 bpm. Heart sound was dull and no murmur could be heard. Abdomen wall was soft, liver and spleen could not be palpated on sub-costal line. ECG demonstrated sinus rhythm with frequent ventricular extrasystoles and pathological Q waves along with 0.2-0.7 mV ST segment elevation in leads V_1-V_5. Coronary angiogram was performed 3.5 hours after onset of symptoms and revealed a 95% eccentric stenosis at the bifurcation of 1st diagonal (D1) branch of left anterior descending (LAD) (A, B in figure 1) with a grade-2 TIMI flow and a 60% stenosis at the proximal segment of right coronary artery (RCA) (C in figure 1). During angiography of RCA, delayed washout of contrast medium occurred, rhythm monitor showed Ⅲ° AVB, and ventricular rate once dropped to 20 bpm with dizziness. After immediate withdrawal of catheter, abnormal changes disappeared and the patient resumed stable condition 30 seconds later. We inferred that it was due to spasm of RCA induced by manipulation of catheter. Coronary intervention: a 3.0mm × 15mm Medtronic S7 stent was deployed at the proximal segment of LAD, and angiographic reexamination after stenting displayed complete abolishing of stenosis without dissection, TIMI flow returned to grade 3, while the stenosis of D1 remained intact (D, E in figure 1). After intervention, chest pain palpitation, heavy breath or nocturnal paroxysmal dyspnea disappeared. The patient began to do daily activities at ease 2 days later, and was discharged 7 days later.

Clinical Discussion

Dr. Zhang Haibin: With ageing of the population, the number of elderly patients presenting acute myocardial infarction (AMI) will continue to increase. In USA alone, this group increased from 21 millions in 1990 to over 25 millions in 1999, and is predicted to reach nearly 36 million people by the year 2020. Elderly patients are likely to have more contraindications and complications to thrombolytic therapy, and more adverse hemodynamic and angiographic predictors of poor outcome than younger patients.

Elderly patients have a documented increase in bleeding complications (including intracranial hemorrhage) and mortality with thrombolytic therapy. In the GUSTO [Global Utilization of Streptokinase and Tissue-type Plasminogen Activator (t-PA) for Occluded Coronary Arteries] Ⅰ trial, the 30-day mortality rates after thrombolysis for patients aged 65-74, 74-85 and > 85 years were 9.5%, 19.6% and 30.3%, respectively. Thiemann, *et al* compared the risks and benefits of intravenous thrombolysis in patients aged 65-75 years with those in patients aged 76-86 years, the results showed that there was a 30-day survival benefit in the younger patients (hazard ratio 0.76, 95% confidence interval 0.61-0.95) and worsened survival in the older group (hazard ratio 1.29, 95% confidence interval 1.06-1.58), with mortality rate reducing from 9.8% to 6.8% in the younger group but increasing from 15.4% to 18% in the older one. Further analysis showed that death began to increase with thrombolysis after age of 74.3 years. Increased rates of intracranial hemorrhage and cardiac rupture in the older patients may explain the lack of benefit of thrombolytic therapy in these persons. The present patient is 81 years of age, although treated within 6 hours after onset, he would not be an ideal candidate for thrombolysis.

Dr. Zhang Xuekun: Many of the early trials of thrombolytic therapy intentionally excluded patients aged 75 years or older because of a perceived increase in bleeding and overall mortality. Later trials began to include these patients, and especially those for comparing thrombolytic therapy with primary percutaneous coronary intervention (PCI), but the average age in many of these trials remained to be approximately 60 years.

There has been no head-to-head trial of thrombolytic therapy *versus* primary PCI in this patient cohort, but there are indications from previous trials that primary PCI is likely to be the superior therapy for aged AMI patients. Most elderly patients are candidates for primary PCI, but many have contraindications to thrombolytic therapy. GUSTO Ⅱb trial showed that the outcome of angioplasty was always superior to that of t-PA for each 10-year patient group (50-59 years, 60-69 years, *etc*). In the Primary Angioplasty in Myocardial Infarction (PAMI)-Ⅰ Trial, the benefit of percutaneous transluminal coronary angioplasty (PTCA) over t-PA was marked in patients aged more than 65 years, with a reduction in the 6-month composite endpoint of in-hospital death and reinfarction from 20% to 8.6% ($P<0.05$). So, I do think that PCI may be a rational option for the present case, the potential risk lies in the fact that he had low blood pressure, suspecting cardiogenic shock.

Dr. Ma Changsheng: According to the data from National Center for Health Statistics of the USA, nearly 1/3 of AMI occurred in patients older than 75 years of age. Pooled data analysis also showed that more than 60% of all deaths from AMI occurred in patients older than 75 years. Patients older than 75 years were more likely to have a history of hypertension, diabetes mellitus, congestive heart failure, previous coronary revascularization (PCI or bypass surgery), peripheral vascular disease, stroke, or chronic obstructive lung disease. With the gradual ageing process, elderly patients presenting an ST-segment elevation AMI will continue to increase, and more care should be paid to such patients. Regarding the management of such patients, importance should be attached to the following issues based on the case mentioned above.

1. Thrombolysis or primary PCI?

Reperfusion treatment for patient with ST-segment elevation AMI is to open the infarct-related artery (IRA) to regain antegrade blood flow, and it can be achieved with either thrombolysis or direct PTCA. Since the first application of direct PTCA in AMI by Meyer, *et al* in 1982, several randomized trials have been conducted, demonstrating a more than 90% success rate of direct PTCA to regain antegrade blood flow, much higher than that of thrombolysis. Meta data analysis (10 trials, total 2 606 patients included) by Weaver. *et al* showed that the 30-day mortality and the composite endpoint of death, nonfatal myocardial infarction and stroke in PTCA group was much lower than those in the thrombolytic one, and it is well recognized that direct PTCA is superior to

thrombolyisis in many aspects. Compared with PTCA, intra-coronary stenting can further improve short-term and long-term benefits.

The investigation from Fibrinolytic Therapy Trialists (FTT) Collaborative Group indicated that, of all patients with AMI, 18 lives could be saved per 1 000 patients treated with thrombolysis. For patients older than 75 years old, benefits from thrombolysis declined. But in spite of the lower amplitude of mortality reduction in patients older than 75 years, about 10 deaths could be prevented among 1 000 patients treated with thrombolysis. It should also be noted that thrombolytic treatment was associated with intracranial hemorrhage, mostly occurred on the 1st day after thrombolytic therapy, and age older than 65 years was a major risk factor for intracranial hemorrhage.

Pooled analysis of PAMI trials comparing AMI patients younger than 75 years old with those older showed that the success rate of PCI and TIMI flow grading were lower for the elderly, whereas the in-hospital mortality (10.2% *vs* 1.8%, $P=0.001$) and complication rate were higher. But when compared with thrombolytic therapy, PCI presented equal or greater benefits. Large-scale registry National Registry of Myocardial Infarction (NRMI)-2 showed that among patients older than 75 years old, mortality of PTCA group and thrombolytic group was almost the same, and it implied that, for elderly patients with AMI, efficacy of direct PTCA is at least equal to thrombolysis. In Primary Angioplasty of Myocardial Infarction Trial (PAMI), direct PTCA could significantly reduce in-hospital death and re-infarction as compared with thrombolytic therapy. Decreased rate of intracranial hemorrhage may partially contribute to the superiority of primary PTCA, because the cardiac death rate was comparable in both groups. In the ZWOLLE Myocardial Infarction study, the 30-day mortality (4% *vs* 29%), 1-year mortality (13% *vs* 44%) and rate of adverse events (death, re-infarction, stroke) in patients older than 75 years old receiving direct PTCA were significantly lower than those of the thrombolytic group.

The present case has anterior wall MI with a short duration between onset of symptoms and admission, timely reperfusion treatment may be a beneficial choice. As to the advanced age of 81 years, the net benefit of thrombolysis may be limited, with increased risk of intracranial hemorrhage. Direct PTCA is safe and efficacious with good immediate result, and is well indicated for patient at high risk of bleeding or patients contraindicated to thrombolysis.

2. Primary PCI for elderly patients at low risk?

There is a discrepancy regarding the revascularization for patients with AMI older than 80 years at low risk. Minai, *et al* randomized 120 patients (no stroke within 6 months, no severe valvular disease, no left bundle branch block and permanent pacemaker, no chronic renal failure, no ventricular septal defect, no cardiogenic shock) older than 80 years old into direct PTCA group and thrombolytic one respectively. After 3 years of follow-up, direct PTCA group presented no obvious improvement in survival rate or reduction in adverse events. Direct PTCA at early stage could not prevent left ventricle from remodeling. But owing to the limited sample size and the non-stent background, the trial results should be dealt with cautiously. The value of risk stratification for elderly patients with AMI remains to be explored.

The current case can be regarded as at relatively low risk, since he had no aforementioned risk factors. Although his short-term efficacy after PCI was good, the long-term result remains unknown. He had a lowered blood pressure less than 80 mmHg on admission, no peripheral hypoperfusion could be observed, so diagnosis of cardiac shock could not be established. Decreased blood pressure may be associated with sweating, vomiting, or previous oral medication of vasodilators.

3. Primary PCI for elderly (>75 years) patients concomitant with cardiogenic shock?

According to the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial, for patients younger than 75 years old complicated by cardiogenic shock, reperfusion therapy can reduce 9% and 17% of 30-day and 6-month mortality respectively, the 1-year survival was also improved. For patients with cardiogenic shock,

reperfusion treatment can save 93 lives per 1 000 patients treated. For younger patients, immediate reperfusion treatment can reduce 30-day mortality to less than 50%, and 1-year mortality is only 53%. AMI complicated by cardiogenic shock is the class Ⅰ indication of reperfusion therapy for patients younger than 75 years old (ACC/AHA, 2001).

On the other hand, subgroup analysis of SHOCK trial showed that early revascularization had a much higher 30-day (75.0% *vs* 53.1%), 6-month (79.2% *vs* 56.3%) and 1-year (79.2% *vs* 65.6%) mortality for patients older than 75 years of age, as compared with initial medical stabilization. Only patients younger than 75 years old can benefit from immediate reperfusion treatment.

Though the diagnosis of cardiogenic shock could not be established in the present case, it should be emphasized that once the diagnosis of cardiogenic shock is realized, direct PTCA is not recommended according to the present knowledge (ACC/AHA).

In conclusion, a head-to-head, prospective, randomized study of thrombolytic therapy *versus* primary PCI in elderly patients is warranted. The ongoing Senior PAMI trial will enroll 530 elderly AMI patients, who will be randomized to primary PCI or thrombolytic therapy (t-PA or r-PA) with a primary composite end-point of death or disabling stroke at 30 days. Multiple secondary end-points will be measured at 1, 6 and 12 months. Steady expansion of patient population calls for further subgroup analyses and risk stratification for this patient cohort.

(Translator NIE Shaoping)

(收稿日期:2003-03-14)
(本文编辑:周宇红)

高龄、胸痛、ST 段抬高伴低血压
(第 5 例)

1 病历摘要

患者,男性,81 岁,因"持续性胸痛 2.5h"于 2003 年 1 月 21 日入院。入院前 2.5h 于生气后出现心前区压榨样疼痛,疼痛无放射,持续不缓解,伴胸闷、心悸、大汗、恶心,呕吐胃内容物一次,含服"速效救心丸"等药物无缓解。起病后未小便。既往史:近 1 年时有劳累后心前区疼痛发作。否认高血压及糖尿病史。吸烟 60 年,10～20 支/d。慢性支气管炎 2 年。体格检查:血压 62/45mmHg(1mmHg = 0.1333kPa),神志清楚,痛苦面容,自动体位,四肢温暖。双侧颈静脉无充盈。双肺呼吸音粗,可闻及少许干啰音。心界叩诊不大,心率 75 次/min,律不齐,可闻及早搏,约 10 次/min,心音低钝,未闻及杂音。腹软,肝脾未及,双下肢无水肿。心电图:窦性心律,频发室性早搏,V_1-V_5 病理性 Q 波,ST 段弓背向上抬高0.2～0.7mV。症状发作 3.5h 后行冠状动脉造影,示前降支近段 D1 分叉处 95%偏心局限性狭窄(图 1A,1B),TIMI 血流 2 级,右冠近段 60%狭窄(图 1C),右冠脉造影过程中出现造影剂排空延迟,立即撤出造影管,心电监护提示Ⅲ°房室传导阻滞,心室率一度减慢至 20 次/min,当时患者诉头晕,无晕厥抽搐等,30s 后自行好转,考虑造影导管刺激导致右冠脉痉挛所致。在 LAD 近段植入 3.0mm×15mm Medtronic S7 支架(12atm),复查造影狭窄消失,TIMI 血流恢复至 3 级,无残余狭窄及夹层形成,D1 开口狭窄未明显加重(图 1D,1E)。术后胸痛消失,无心悸、喘憋,无夜间阵发性呼吸困难,2d 后下床活动,日常活动无不适,7d 后出院。

2 临床讨论

张海滨医师:伴随着人口的老龄化,老年急性心肌梗死(acute myocardial infarction, AMI)呈逐渐增加的趋势。仅在美国,老年 AMI 患者就从 1990 年的2 110万增加到 1999 年的 2 500 万,预计 2020 年将达到 3 600 万。与年轻患者相比,老年患者溶栓治疗的禁忌证、合并症,以及预测不良结果的血流动力学与冠状动脉造影特征更多。

老年患者接受溶栓治疗后出血(包括脑出血)并发症和死亡率增加。GUSTO-1 试验表明,年龄为 65～74岁,74～85岁和≥85岁的患者溶栓治疗30d

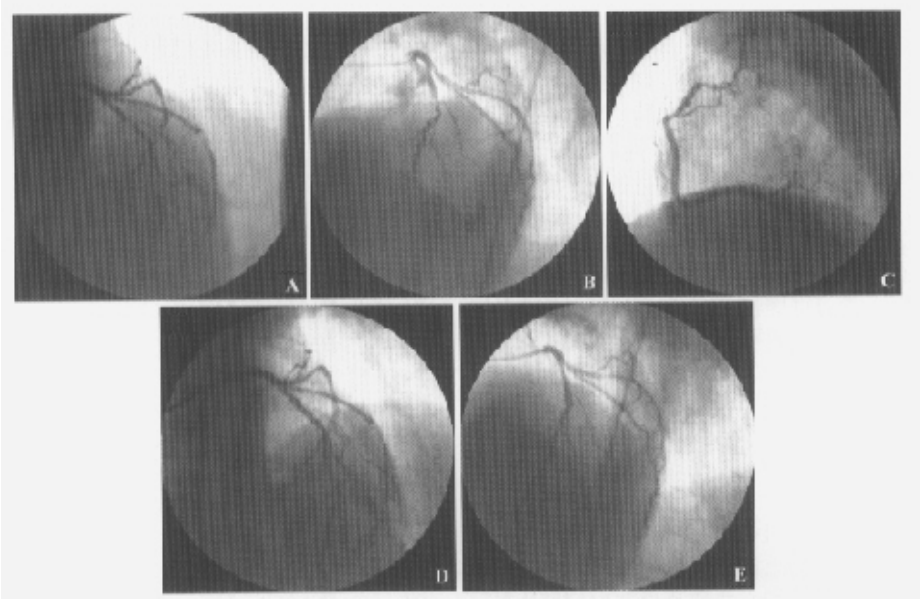

图 1 冠状动脉造影图

A,B:前降支近段 D1 分叉处 95%偏心局限性狭窄;C:TIMI 血流 2 级,右冠状动脉近段 60%狭窄;D,E:复查造影狭窄消失,TIMI 血流恢复至 3 级,无残余狭窄及夹层形成,D1 开口狭窄未明显加重

死亡率分别为 9.5%,19.6%和 30.3%。Thiemann 等比较年龄为 65～75 岁和 76～86 岁患者静脉溶栓治疗的风险与得益发现,年龄较轻患者的 30d 生存率更高(风险率 0.76,95%可信限 0.61～0.95),反之,年龄较大患者生存率降低(风险率 1.29,95%可信限 1.06～1.58);年轻患者的死亡率由 9.8%降至 6.8%,而年龄较大患者则由 15.4%升高至 18%。分析发现,>74.3 岁患者接受溶栓治疗死亡率开始增加,可能与颅内出血与心脏破裂增加有关。此患者为 81 岁高龄患者,尽管 AMI 发作<6h,溶栓治疗显然并不适宜。

张学坤医师:考虑到发生出血与死亡的危险均较大,早期有关溶栓治疗的临床试验均未入选≥75 岁的高龄患者。尽管最近的部分临床试验,尤其是比较溶栓治疗与直接经皮冠状动脉介入(percutaneous coronary intervention, PCI)的临床试验,开始入选老年患者,但其平均年龄一般在 60 岁左右。

对于高龄患者,目前尚无比较溶栓治疗与直接 PCI 的大型临床随机试验。然而,先前的临床试验提示,高龄 AMI 患者直接 PCI 可能更好。尽管多数老年 AMI 患者存在溶栓治疗的禁忌证,但绝大多数患者仍适合 PCI 治疗。GUSTO-Ⅱb 试验发现,在每 10 岁年龄段中(如 50～59 岁,60～69 岁等),PCI 的结果均优于组织型纤溶酶原激活剂(tissue-type ptasminogen activator, t-PA)溶栓治疗。PAMI-1 试验显示,≥65 岁的患者经皮冠状动脉球囊成形术(percutaneous transluminal coronary angioplasty, PTCA)的得益明显大于 t-PA 溶栓,能将 6 个月的复合终点(住院死亡和再梗死)由 20%降至 8.6%(P<0.05)。因而,该患者可能更适合介入治疗。但该患者 PCI 也有潜在风险,因存在低血压,需要除外心原性休克。

马长生医师:根据美国国立健康统计中心(National Center for Health Statistics)的资料,大约 1/3 的 AMI 发生于≥75 岁的老年患者。PAMI 试验汇总分析表明,在因 AMI 导致的所有死亡患者中,≥60%的患者年龄≥75 岁。≥75 岁的高龄患者,高血压、糖尿病、充血性心力衰竭、既往血运重建(PCI 或冠状动脉搭桥术)冠状动脉、外周血管疾病、卒中和阻塞性肺病等更为多见。随着人口的逐步老龄化,老年人发生 ST 段抬高 AMI 将日渐增多,应引起足够重视。结合本例患者,有关老年人 AMI 的处理主要应注意以下几个问题:

(1)溶栓治疗还是直接 PCI?

急性 ST 段抬高性心肌梗死的再灌注治疗旨在开通梗死相关动脉,恢复其前向血流,主要包括溶栓治疗和直接 PTCA 两种手段。1982 年,Meyer 等首次应用直接 PTCA 治疗 AMI,以后的几项随机研究

显示，PTCA 恢复冠脉前向血流的成功率均≥90%，高于溶栓治疗。Weaver 等对 10 项研究中的 2 606 例 AMI 患者进行荟萃分析显示，PTCA 组 30d 死亡率、死亡与非致死性心肌梗死率及脑卒中发生率明显低于溶栓组，直接 PTCA 优于溶栓治疗。与单纯 PTCA 相比，冠脉内支架进一步改善了近期及远期临床结果。

FTT 协作组(Fibrinolytic Therapy Trialists Collaborative Group)研究表明，在所有 AMI 患者中，每 1 000例接受溶栓可以挽救 18 个生命；但是，年龄≥75 岁的患者溶栓治疗的相对益处降低，其死亡率的降低幅度低于＜75 岁的患者，但每治疗 1 000 例患者仍可以减少 10 人死亡。溶栓治疗与发生在治疗首日的脑卒中危险增高有关，＞65 岁是颅内出血危险增加的主要临床因素之一。

PAMI 试验汇总分析表明，与＜75 岁的 AMI 患者相比，≥75 岁的患者 PCI 的成功率和 TIMI 3 级血流率均较＜75 岁的患者低，住院死亡率(10.2% *vs* 1.8%，$P=0.001$)和心肌梗死后并发症发生率却更高。然而，与溶栓治疗相比，老年 AMI 患者直接 PCI 的疗效仍等同于甚至优于溶栓治疗。NRMI-2登记提示，年龄≥75 岁的患者，直接 PTCA 与溶栓治疗的死亡率相当，这说明在高龄 AMI 患者中，PTCA 的疗效及安全性至少与溶栓治疗相当。PAMI 试验发现，在≥65 岁的 AMI 患者中，直接 PTCA 较tPA溶栓明显降低院内死亡或再梗死的发生率。PTCA改善存活的益处可能部分是来自脑出血合并死亡的发生率低于溶栓组的结果，两组与心脏相关的死亡率相似。ZWOLLE 心肌梗死研究(Zwolle Myocardial Infarction Study)显示，≥75 岁的 AMI 患者直接 PCI 的 30d(4% *vs* 29%)与 1 年(13% *vs* 44%)不良事件(死亡、再梗死与卒中)发生率均显著低于链激酶溶栓。

本例患者到院时距发病时间短(2.5h)，又为前壁心肌梗死，及时进行再灌注治疗可使患者最大限度受益。但患者是 81 岁的老年患者，溶栓所获得的益处可能相对不大，并显著增加出血性脑卒中的危险。直接 PTCA 不但即刻效果好，而且较为安全，适合于这种出血风险高、有溶栓治疗禁忌证的患者。

(2)低危高龄患者是否直接 PCI?

≥80 岁的低危 AMI 患者能否从直接 PCI 获益尚有争议。Minai 等将 120 名≥80 岁的低危(6 个月内无卒中、无严重瓣膜病、无左束支阻滞或永久起搏器、无慢性肾功能衰竭、无室间隔缺损、无心原性休克)AMI 患者随机分为直接 PTCA(无支架)和保守治疗两组，随访 3 年发现，直接 PTCA 组生存率改善和不良事件减少并不明显，早期 PTCA 也未能防止心肌梗死后的左心室重构。然而，该研究存在例数较少、未使用支架等缺点，危险分层与高龄 AMI 患者直接 PTCA 的关系有待于深入研究。

本例患者无上述高危因素，直接 PTCA 术后近期效果良好。患者入院时虽然血压＜80mmHg，但没有周围循环灌注不足的表现，所以不能诊断为心原性休克。其低血压可能与大汗和呕吐后血容量降低及自行服用血管扩张剂有关。

(3)≥75 岁患者 AMI 合并心原性休克是否直接 PCI?

SHOCK 试验表明，对于＜75 岁的合并心原性休克的患者，血运重建治疗能使 30d 死亡率降低 9%，6 个月死亡率明显降低 17%，并能明显提高 1 年生存率。每 1 000 名心原性休克患者接受血运重建治疗可以挽救 93 个生命。对于非老年患者，早期血运重建治疗使心原性休克的 30d 死亡率降低至＜50%，1 年死亡率仅 53%左右。AMI 合并心原性休克是血运重建治疗的Ⅰ类适应证(ACC/AHA，2001)。

然而，SHOCK 试验亚组分析表明，≥75 岁的患者接受早期血运重建治疗后 30d(75.0% *vs* 53.1%)、6 个月(79.2% *vs* 56.3%)和 1 年(79.2% *vs* 65.6%)的死亡率明显高于初始药物治疗(initial medical stabilization)，只有＜75 岁的患者能从早期血运重建中明显受益。

尽管本例患者不能确诊心原性休克，然而，一旦确诊心原性休克，根据 ACC/AHA 有关 PCI 的指南建议，≥75 岁的老年患者，不主张行直接 PCI 治疗，临床对此应予以高度重视。

总之，有关老年人 AMI 的处理还有待于直接比较溶栓治疗与 PCI 的前瞻性随机试验结果进行进一步评价。正在进行中的 Senior PAMI 试验将入选 530 名老年 AMI 患者，随机接受直接 PCI 和溶栓治疗〔t-PA 或重组纤溶酶原激活剂(recombinant plasminosen activafor，r-PA)〕，主要终点指标为 30d 死亡和致残性卒中的发生率，该试验还包括 1，6，12 个月等一系列次级终点等。随着老年患者的逐渐增加，进一步进行亚组分析与危险分层研究也具有重要意义。

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(收稿日期：2003-02-24)

(本文编辑：周宇红)