Peer reviewed article

Safety and outcome of patients with an acute ST-elevation myocardial infarction transferred for primary coronary intervention: the Neuchâtel experience

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Summary

Background: Transferring patients with ST-elevation myocardial infarction (STEMI) for primary percutaneous coronary intervention (PCI) from a community hospital to a PCI centre has been evaluated in randomised trials and shown to be safe and effective. A prolonged transfer time may restrict the benefit of this strategy.

Aim: We sought to assess 1) safety of transfer from Neuchâtel to Berne, 2) time intervals of patients transferred either directly from on-site or after evaluation in the local emergency room, and 3) clinical long-term outcome.

Methods and results: 42 patients with STEMI eligible for reperfusion therapy were prospectively included between January 2003 and June 2004. Twenty patients (48%, group 1) were directly transferred to the PCI centre from on-site. Twenty-two were transferred after initial treatment in the local emergency room: 11 patients (26%, group 2) presented spontaneously at the hospital and 11 patients (26%, group 3) were admitted by the rescue team. No major complication occurred during transport. Median transport time was 33 minutes. Median time from first healthcare contact to balloon consisted of 131 minutes in group 1, 158 minutes in group 2 and 174 minutes in group 3. The overall rate of Major Adverse Cardiac Events (MACE) at 6 months amounted to 9.5%.

Conclusions: Transfer for primary PCI of our patients with acute STEMI was safe. Direct transfer from on-site to the PCI centre reduced the time of ischaemia. The overall MACE rate was low.

Keywords: acute myocardial infarction; STEMI; PCI; transfer; reperfusion strategy

Introduction

A review of 23 randomised trials comparing pharmacological to mechanical reperfusion therapy in acute ST-Elevation Myocardial Infarction (STEMI) has demonstrated superiority of Percutaneous Coronary Intervention (PCI) in reducing overall death, re-infarction and stroke [1–2]. This also holds true for patients who need to be transferred from a community hospital to a PCI centre with a significant reduction of re-infarction, stroke and the combined end point of Major Adverse Cardiac Events (MACE) in the PCI group [3–7].

The principle "time is muscle" confers to patients treated with fibrinolytics as well as to patients undergoing primary PCI. Previous data showed a direct relationship of symptom onset-to-balloon time and door-to-balloon time with mortality [8]. Therefore, the current guidelines of the European Society of Cardiology and the American Heart Association for the management of STEMI stipulate that the delay of medical contact-to-balloon or door-to-balloon should be less than 90 minutes [9–10]. For all patients presenting later than 3 hours after onset of pain, primary PCI is recommended unless a delay to invasive strategy is likely to be longer than 2–3 hours. To achieve these recommended guidelines, an extensive interdisciplinary collaboration is required [11]. Fibrinolysis is a viable alternative if the patient presents

Abbreviations

PCI = Percutaneous Coronary Intervention
STEMI = ST-elevation myocardial infarction
MACE = Major Adverse Cardiac Events
CABG = Coronary Artery Bypass Grafting
ACLS = Advanced Cardiac Life Support
SMUR = Service Mobile d'Urgence et de Réanimation

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very early, within 3 hours after onset of symptoms [9] to a centre without catheterisation laboratory.

The district of Neuchâtel has a recruitment basin of 170,000 inhabitants, and the Hôpital Cadolles-Pourtalès covers about 100,000. The district does not offer a cardiac catheterisation laboratory and the nearest centre with an emergency PCI service around the clock for 365 days per year is the Swiss Heart Centre, Inselspital in Berne, at a distance of 50 km from Neuchâtel. Based on the superiority of primary PCI compared to thrombolysis for the majority of patients, the medical department of the Hôpital Cadolles-Pourtalès in Neuchâtel has adopted the strategy to transfer patients with acute STEMI for invasive reperfusion therapy as standard treatment since January 2003. To assess the quality of this treatment strategy, we prospectively included all patients with STEMI transferred for primary PCI during an 18 months period. We aimed to assess the safety of transfer, the different time intervals and the clinical outcome (MACE).

Methods

Inclusion criteria

Between January 2003 and June 2004, all patients presenting with a STEMI at the emergency room or on a pre-hospital level were evaluated for a transfer to the PCI centre. Diagnosis of STEMI was made according to international guidelines [10]. A 12 leads ECG was performed either on-site by the pre-hospital medical physician or in the emergency room.

Exclusion criteria

Duration of symptoms till health care contact more than 12 hours, uncontrolled haemodynamic and/or respiratory failure, age >85 years and major co- morbidities (patients with severely reduced life expectancy). Secondary exclusion criteria at the PCI centre: patients were secondarily withdrawn from analysis if the physician responsible for PCI concluded that criteria for emergency revascularisation were no more/not fulfilled.

Assignment of groups

Group 1: patients directly transferred to the PCI centre from on-site; Group 2: patients presenting spontaneously at the hospital Cadolles-Pourtalès and being transferred as soon as possible; Group 3: patients being admitted to the hospital Cadolles-Pourtalès by the rescue team for different reasons (ambiguous history, cardiopulmonary instability, logistic problems) and transferred after assessment in the emergency department.

Standard treatment protocol before/during transfer

After confirming the diagnosis of acute STEMI with a 12 leads ECG and excluding contraindications, classical anti-ischaemic treatment (acetylsalicylic acid 500 mg i.v.; clopidogrel 300 mg loading dose; heparin bolus 60 U/kg i.v. or enoxaparin 30 mg i.v. followed by 1 mg/kg s.c. in patients without regular coumarine treatment; metoprolol 3×5 mg i.v. in absence of classical contra-indications; morphine 0–10 mg i.v.; nitroglycerin 0.8–1.6 mg s.l.) was started immediately. The pre-hospital medical team (SMUR: Service Mobile d'Urgence et de Réanimation) was immediately dispatched to the site of emergency if typical chest pain was reported to the emergency central. The SMUR physician performed initial diagnostic and therapeutic work-up on-site. By phone, he/she checked the indication for transfer and emergency PCI for all patients with the senior physician in charge of the medical emergency department of the hospital Cadolles-Pourtalès. The PCI team was informed immediately by this senior physician and so had time to get ready while a physician trained in advanced cardiac life support (ACLS) accompanied the patient to the PCI centre.

Data collection

The following patient characteristics were recorded: age, sex, cardiovascular risk factors, acute treatment, extent of coronary artery disease, arrhythmia (ventricular tachycardia, ventricular fibrillation, asystoly, AV-blocks/extreme bradycardia), time of symptom onset, time of first call, time of first rescue healthcare contact (ambulance, SMUR or local hospital), time of departure for transfer, time of arrival at local hospital/at PCI centre, time of balloon inflation, type of reperfusion (PCI or CABG), length of stay in hospital, MACE (unscheduled revascularisation, re-infarction, stroke and death) at 30 days and 6 months (as determined by a telephone interview with the responsible physician or the patient).

Statistics

Numerical values are given as median and range. Categorical values are given as numbers and percentage. The first goal of this study was a control of quality of our STEMI management. The study itself was not designed and powered to detect a difference between the groups. Therefore no p values are given.

Results

A total of 48 patients (figure 1) were transferred for primary PCI during the 18 months study period. 6 of these patients did not undergo emergency but elective angiogram, as the physician responsible for PCI did not confirm the indication for emergency revascularisation. These patients were withdrawn from analysis.

Of the 42 patients undergoing emergency coronary angiography, 20 (48%) had been transferred from the site of emergency to the PCI centre (group 1). 11 (26%) had arrived on their own at the hospital Cadolles-Pourtalès (group 2) and 11 (26%) were admitted by ambulance to the emergency room of Cadolles-Pourtalès, before being

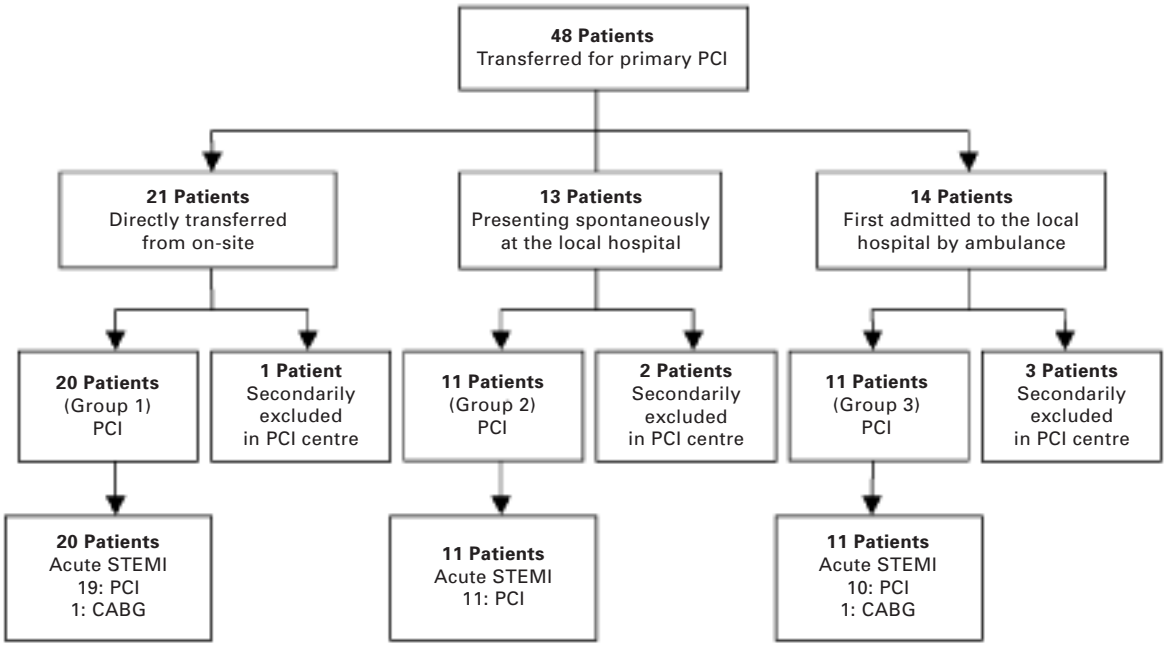

Figure 1

Assignment of groups and treatment.
PCI: Percutaneous Coronary Intervention
STEMI: ST-Elevation Myocardial Infarction
CABG: Coronary Artery Bypass Grafting

Table 1

Baseline characteristics.

	Group 1 n = 20	Group 2 n = 11	Group 3 n = 11
Number of Patients	20 (48%)	11 (26%)	11 (26%)
Age (years, median)	60	55	65
Male (%)	75	82	82
Hypertension (%)	50	55	64
Diabetes (%)	15	9	18
Smoking (%)	55	64	55
Known CAD[a] (%)	35	18	9
Extent of disease (%)			
One-vessel disease	35	55	36
Two-vessel disease	40	27	46
Three-vessel disease	25	18	18
Acute treatment[b] (% of patients):			
Aspirin	100	100	100
Clopidogrel	75	73	46
Beta-blockers	70	82	73
Heparin/Enoxaparin	100	91	91
Nitrates	95	82	82

Group 1: Direct transfer for PCI
Group 2: First presentation at local hospital then transfer for PCI
Group 3: By ambulance to local hospital then transfer for PCI
a) coronary heart disease (CAD), including history of infarction, angina or previous PCI
b) before arrival at PCI centre

transferred for primary PCI (group 3). All these 42 patients underwent either PCI (n = 40) or urgent CABG (n = 2). Baseline characteristics are listed in table 1 and were comparable between the groups.

Safety of transfer

No major complication such as ventricular fibrillation, cardiogenic shock or death occurred during transport to the PCI centre. One patient developed a 2nd degree AV block but remained haemodynamically stable without intervention. One patient initially presented with an acute pulmonary oedema and one with cardiogenic shock. Both were stabilised by medical treatment and then transferred without complications. Of note, *before* departure, 3 patients presented ventricular arrhythmias (1 ventricular tachycardia and 2 ventricular fibrillations) that were successfully treated by defibrillation. None of these 3 patients presented further problems during transport.

Time intervals

The different time intervals for each group are shown in table 2 and illustrated in figure 2. The time interval "first healthcare contact-to-balloon" for each group is shown in figure 3.

Outcome

Mortality and MACE at 30 days and 6 months are listed in table 3. One cardiac death occurred within the first month, another one after 5 months (complication after heart transplantation for end-stage heart failure). No re-infarction and no stroke were recorded during the follow-up. The median hospital length of stay was 8 days in all three groups.

Discussion

Our study aimed to assess the quality of management of patients with an acute STEMI. First, our observational data are in line with previous randomised controlled trials evaluating transfer PCI versus fibrinolytic therapy with regard to complication rate: the highest rate of 1.2% was

Figure 2

Time intervals. Flow-chart illustrating the different steps in groups 1–3.

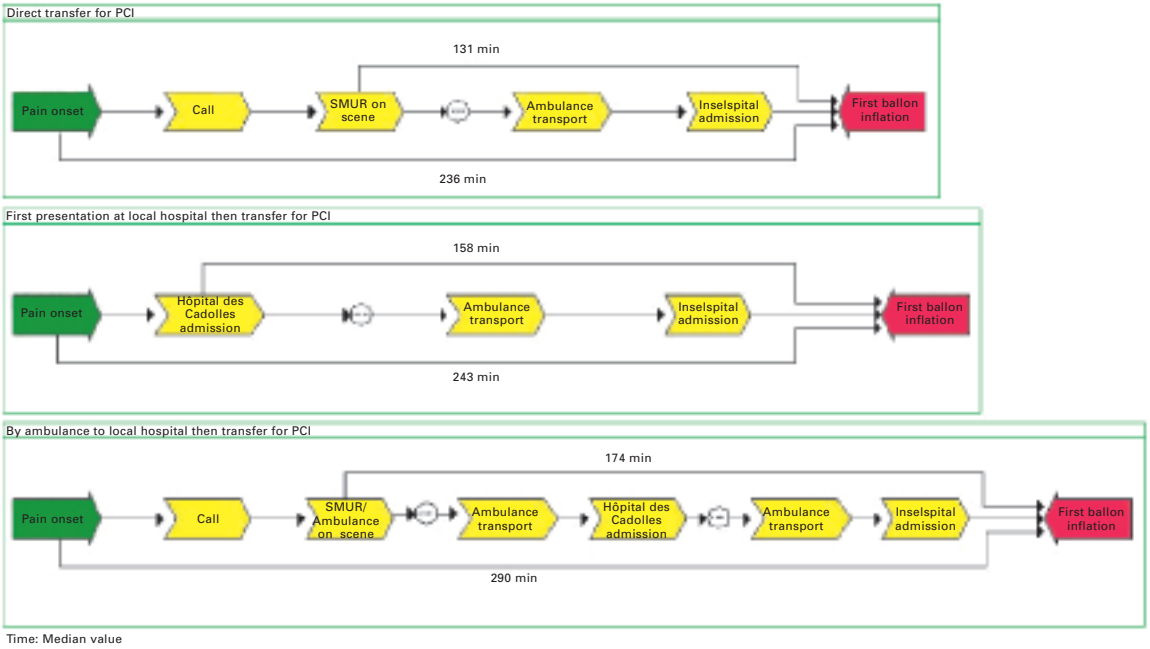

Table 2

Time intervals.

Intervals	Group 1 n = 20	Group 2 n = 11	Group 3 n = 11
From onset of symptoms to hospital admission	NA	43 (15–270)	124 (40–758)
From onset of symptoms to arrival of SMUR[a]	75 (31–543)	NA	83 (22–320)[b]
From hospital admission to start of transfer	NA	70 (34–139)	65 (5–141)
From arrival of SMUR to start of transfer	40 (10–60)	NA	NA
Transport duration	36 (23–57)	31 (26–37)	30 (30–41)
From arrival at PCI centre to balloon	49 (27–121)	46 (34–190)	43 (26–53)
From beginning of PCI to first balloon inflation	24 (10–65)	21 (7–71)	19 (8–33)
From first healthcare contact to balloonc	131 (99–166)	158 (124–285)	174 (116–279)
From onset of symptoms to first balloon inflation	236 (141–707)	243 (154–461)	290 (141–436)

Time given in minutes: median value (min; max)
Group 1: Direct transfer for PCI
Group 2: First presentation at local hospital then transfer for PCI
Group 3: By ambulance to local hospital then transfer for PCI
a) SMUR: pre-hospital medical team
b) SMUR intervention for 6 patients of this group
c) Group 1: from arrival of SMUR; Group 2: from hospital admission and Group 3: from arrival of SMUR (6 patients) or from arrival of ambulance (5 patients)
NA: not applicable

described in PRAGUE-2, probably due to a markedly longer transportation time than in DANAMI-2 or Air-PAMI [5–7]. In our small patient population no complication or arrhythmias occurred during transfer. Three patients presented ventricular arrhythmias *before* departure that needed intervention. Furthermore, one patient with cardiogenic shock and another with acute pulmonary oedema were transferred safely after initial stabilisation on site. The fact that 5 out of 42 patients presented life-threatening complications in the early phase of treatment underscores the necessity of a physician experienced in ACLS accompanying the transfer. In general, no definitive statement can be made with respect to safety due to this small number of patients in our patient population. The large prospective studies however indicate, that complications during transfer are rare [5–7]. As safety is a strong matter of concern, we nevertheless recommend accompanying the patient with a physician trained in advanced life support.

Second, transfer times in our observational study were comparable to large randomised trials: median transport time amounted to 33 minutes in our study, 32 minutes in DANAMI-2, 48 minutes in PRAGUE-2 and 26 minutes in Air-PAMI, respectively. A direct transfer from on-site directly to the catheterisation laboratory lead to a "first health-care contact to balloon time" of 131 minutes, including 36 minutes of transportation and resulted in a 24% reduction of this time interval in group 1 compared to group 3. The importance of keeping time of ischaemia as short as possible has been described previously and a direct relationship of door-to-balloon time and mortality was re-

Table 3
MACE.

MACE at 30 days	Group 1 n = 20	Group 2 n = 11	Group 3 n = 11
Revascularisation[1]	0	1 (9%)	0
Re-infarction	0	0	0
Stroke	0	0	0
Death	1 (5%)	0	0
MACE[2]	1 (5%)	1 (9%)	0
MACE at 6 months[3]			
Revascularisation	1 (5%)	1 (9%)	0
Re-infarction	0	0	0
Stroke	0	0	0
Death	2 (10%)	0	0
MACE	3 (15%)	1 (9%)	0

Group 1: Direct transfer for PCI
Group 2: First presentation at local hospital then transfer for PCI
Group 3: By ambulance to local hospital then transfer for PCI
1: Revascularisation includes unscheduled CABG or coronary angioplasty
2: MACE includes revascularisation, re-infarction, stroke and death
3: Evolution at 6 months: all events since inclusion

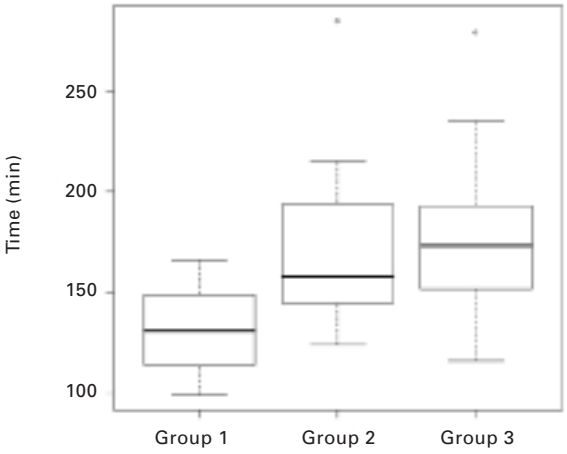

Figure 3
Delay from first healthcare contact to balloon inflation.
Group 1: From arrival of SMUR to balloon inflation.
Group 2: From arrival at local hospital to balloon inflation.
Group 3: From arrival of SMUR or ambulance to balloon inflation.

ported in a large cohort by Cannon and co-workers [8]. They pointed out that the door-to-balloon time should not exceed 120 minutes, since the mortality increased significantly beyond that time. The current European and American Guidelines for the management of patients with STEMI [9, 10] recommend a time from first health-care contact to balloon of no longer than 90 minutes. This goal, however, is only rarely achieved in real life. For example, the American National Registry of Myocardial Infarction (patients with STEMI included from January 2002 to December 2002) showed that only 3.0% of patients are treated by primary PCI within 90 minutes [12]. In the same registry, the median door-to-balloon time amounted to 185 minutes. In randomised studies comparing transfer for primary PCI with thrombolysis, time interval from first healthcare contact to balloon inflation was 95 and 108 minutes respectively in the groups B and C of PRAGUE, 108 minutes in DANAMI-2 and 155 minutes in Air-PAMI. The intervals of 131 minutes in group 1 and 158 minutes in group 2 of our study are therefore in the range of those measured in these large randomised trials. Even the interval in group 3 was slightly shorter than the median in the American National Registry.

The new 2005 Guidelines of the European Society of Cardiology take the difficulty, to respect the 90 minutes deadline, into account: thrombolysis is recommended only when a substantial delay (>2–3 hours) in initiating PCI is likely [9]. These guidelines further indicate that fibrinolysis is a viable alternative in case of early presentation – within 3 hours after onset of chest pain – and that fibrinolysis and primary PCI are equally effective in reducing infarct size and mortality for patients in this time window. The major reason why primary PCI is preferred to thrombolysis even within the first 3 hours after onset of chest pain is the prevention of stroke. According to these guidelines, primary PCI should be the preferred reperfusion strategy whenever possible for patients presenting between 3 and 12 hours after onset of chest pain, as in these patients primary PCI not only reduced stroke but also saved myocardium [9]. With regard to these latest recommendations, our "first healthcare contact-to-balloon times" in group 1 and 2 can be interpreted as satisfactory, but could still be improved. The interval of 174 minutes from first healthcare contact-to-balloon and the interval of 286 minutes from symptom onset-to-balloon in group 3, respectively, appear too long. This can be explained by the longer interval "onset of symptoms-to-call", and the often complex or ambiguous history of these patients (initially unstable patients, atypical presentation of chest pain that did not warrant the intervention of the SMUR, and/or delay in the diagnosis of STEMI). Establishing the right diagnosis in ambiguous patient history, starting immediate treatment and preparing for safe ambulance transport in unstable patients, however, still needs a certain time. Nevertheless, the SMUR team on the one hand and the team in the emergency department on the other hand are encouraged to make constant efforts to shorten the respective intervals.

A detailed analysis of our time intervals revealed that a gain can be obtained by transferring patients directly from on-site: the reduction in delay to treatment was 27 minutes for group 1 compared to group 2 and 43 minutes for group 1 compared to group 3, respectively. Our findings are in line with two recently published trials [13–14]. Delay to treatment in these studies was 81 and 31 minutes shorter in the group directly transferred compared to the group of patients arrived by themselves at the local hospital. Whenever possible, the transit by the local hospital should therefore be avoided.

The median delay from arrival at PCI centre to balloon of all included patients consists of 47 minutes and seems relatively long. It comprises transfer from ambulance to the catheterisation laboratory, sometimes waiting at the catheterisation laboratory entrance depending on the occupancy, installation in the catheterisation laboratory and

the procedure until the balloon is successfully inflated. We are aware that constant efforts have to be made to optimise interdisciplinary and logistic collaboration also in this setting. The median needle-to-balloon time (from beginning of PCI to reperfusion) was 22 minutes. This delay can be explained by a frequent use of a protection device that should avoid distal embolisation of thrombotic material but prolongs the "needle-to-balloon" time.

Furthermore, the median delay between onset of symptoms and first healthcare contact is 70 minutes, with a very wide range of 15 to 729 minutes. Still too many patients do not dare to call a physician in the middle of the night and/or are not aware of the risk associated with ischaemic chest pain. It is necessary to sensitise the lay public to reduce this very important interval and therefore the total ischaemic time, especially as the latter is directly correlated with 1-year-mortality [15].

Finally, the overall rate of MACE of our 42 patients at 6 months consisted of 9.5% and is well comparable to previous large acute PCI studies [3–7]. Hospital length of stay was short, considering that it includes the whole diagnostic and therapeutic workup, including the stay in the PCI centre. We therefore consider that our strategy to transfer for primary PCI the patients with STEMI is safe, efficacious and cost-effective.

In conclusion, transferring patients with an acute STEMI for PCI appears to be safe in our local setting, clinical long-term outcome compares well with larger trials, and direct transfer from on-site to the next catheterisation laboratory allows reducing the time of ischaemia.

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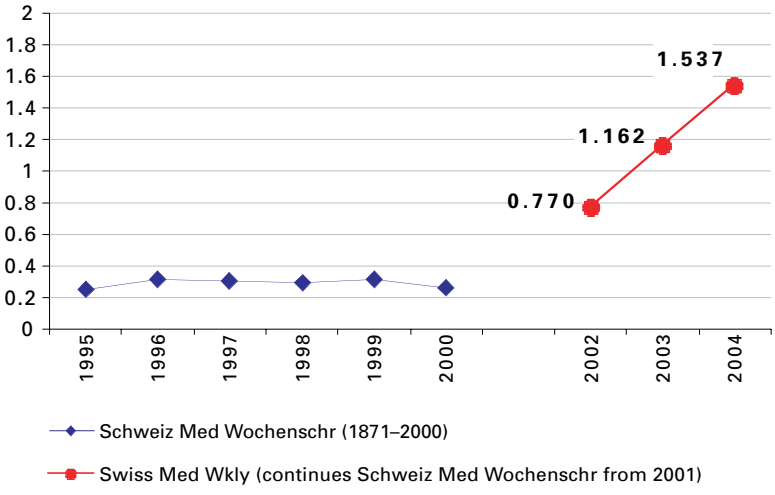

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