Complete percutaneous revascularisation feasibility in ischaemic heart failure is related to improved outcomes: insights from the COMMIT-HF registry

Łukasz Pyka, Michał Hawranek, Mateusz Tajstra, Jarosław Gorol, Andrzej Lekston, Mariusz Gąsior

3rd Department of Cardiology, School of Medicine with the Division of Dentistry in Zabrze, Medical University of Silesia, Katowice, Poland

Abstract

Background and aim: Heart failure (HF) is a major cause of death in cardiovascular disease. In a post-STICH landscape, we lack data on the role of percutaneous coronary intervention (PCI) in systolic HF patients. Complete revascularisation remains a key unanswered question in ischaemic HF.

Methods: The COMMIT-HF is an ongoing systolic HF registry (inclusion criteria: HF with left ventricular ejection fraction ≤ 35%, exclusion: acute coronary syndrome). A total of 1798 patients were enrolled. A group of patients with multi-vessel coronary artery disease qualified for PCI were selected and divided into complete (n = 188) and incomplete revascularisation (n = 159) groups. Completeness of revascularisation was defined as successful PCI of every angiographically significant lesion in all arteries with a diameter of ≥ 2 mm without a patent surgical graft. Patients were followed up for a period of at least 12 months with all-cause mortality defined as the primary endpoint.

Results: The study groups showed no significant differences in clinical status and echocardiographic parameters, with a lower comorbidity rate in the complete revascularisation group. Procedural characteristics were comparable. There were no significant differences in complication rates. All-cause mortality was significantly lower in the complete revascularisation group after 12-months (6.4% vs. 20.1%, p < 0.001). Multivariate analysis confirmed that achievement of complete revascularisation was an independent factor improving survival (HR 0.39; 95% CI 0.18–0.81, p = 0.01).

Conclusions: Percutaneous coronary intervention can be a safe and feasible method of revascularisation in ischaemic HF. Achievement of complete revascularisation with PCI was related to improved outcomes in the analysed patient population.

Key words: percutaneous coronary intervention, heart failure, coronary artery disease

INTRODUCTION

Heart failure (HF) is a constantly growing global health problem, leading to a common consensus that it has become a global pandemic [1, 2]. The prognosis in this group of patients remains unfavourable. Various studies worldwide demonstrate mortality rates within one year of a HF-related hospitalisation at the level of 17–45% [3]. Coronary artery disease (CAD) is the most important aetiological factor and is expected to remain as such due to the effective treatment of CAD and the ageing of the patient population [3, 4]. However, there is still insufficient information on revascularisation in the HF population. After the STICH trial, coronary artery bypass grafting (CABG) in HF has become the recommended form of revascularisation [5]. Nonetheless, only a minor percentage of patients undergo this procedure. Percutaneous coronary intervention (PCI) has been shown to exceed the number of CABGs in this population, despite the lack of compelling data from contemporary randomised studies [6–8]. Although some reports support the role of complete revascularisation (CR) in the improvement of outcomes both in CABG and PCI patients [9], there is no data on the impact of CR achieved with PCI in systolic ischaemic HF. Therefore, having at our disposal
a population of ischaemic HF patients who underwent PCI in a high-volume cardiovascular centre, we aimed to assess the impact of CR feasibility on prognosis in this population.

**METHODS**

The Contemporary Modalities In Treatment of Heart Failure Registry (COMMIT-HF) is an observational study underway in the Third Department of Cardiology in the Silesian Centre for Heart Diseases in Zabrze, Poland (ClinicalTrials.gov, NCT02536443) [10]. Data collection is patient-based. The registry was approved by the local Ethics Board, and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Informed consent was obtained from all participants.

The study population includes an all-comer adult systolic HF patient population, hospitalised for the first time in our centre with exclusion of acute coronary syndromes at admission for index hospitalisation. For the registry, HF is defined as a set of symptoms resulting from myocardial systolic function impairment, with left ventricular ejection fraction (LVEF) ≤ 35% confirmed in resting echocardiography. Complete patient demographics including medical history, hospitalisation data (diagnostic and therapeutic), and in-hospital results are collected by the attending physician. The attending physician has full access to prior medical records and can consult the patients about their medical history. Long-term follow-up data on mortality and non-fatal outcomes is obtained from the national health care provider. Twelve-month vital status was available for the complete patient population. Patients were treated according to the current Heart Failure Treatment, Myocardial Revascularisation, Cardiac Pacing, and Cardiac Resynchronisation Therapy guidelines.

From January 1st 2009 to December 31st 2013, a total of 1798 patients were enrolled in the COMMIT-HF registry. In this cohort, a subset of 755 patients underwent diagnostic coronary angiography (41.9% of all ischaemic HF patients). Patients qualified for CABG (n = 80), with single vessel disease qualified for PCI (n = 8), and qualified for conservative treatment (n = 320) were excluded from further analyses. Subsequently, 347 patients with multi-vessel disease underwent PCI after qualification either by the heart team (68.01%) or by a joint consensus of the attending cardiologist and the interventional cardiologist regarding the patient’s clinical status and additional test results (in this group 22.76% were post CABG, while 9.23% had non-obstructive CAD in the left main and/or left anterior descending arteries). The patients were then divided regarding achievement of complete revascularisation (CR; n = 188; 54.2% vs. incomplete revascularisation; n = 159; 45.8%; Fig. 1).

For this analysis, an anatomic definition of CR was used. CR was defined as successful PCI of all angiographically significant lesions in all coronary arteries with a diameter of at least 2 mm, without a patent surgical graft. Angiographically significant stenosis was defined as a left main and a proximal left anterior descending artery of ≥ 50% and ≥ 70% in all other coronary arteries. Successful PCI was defined as effective stent delivery with a final Thrombolysis in Myocardial Infarction (TIMI) 3 flow and residual stenosis of less than 20%.

The primary endpoint was 12-month all-cause mortality. Secondary endpoints included in-hospital major adverse
cardiac and cerebrovascular event (MACCE) consisting of all-cause mortality, non-fatal myocardial infarction (defined as an ischaemic event meeting the European Society of Cardiology/American College of Cardiology criteria), cerebrovascular insult (defined as an acute neurologic disorder lasting > 24 h and affecting the ability to perform daily activities or resulting in death), and major bleeding (defined as an overt cranial, intestinal or access site-related bleeding resulting in haemodynamic compromise or requiring blood transfusion), as well as 12-month MACCE consisting of all-cause mortality, non-fatal myocardial infarction, and cerebrovascular insult.

**Statistical analysis**

The continuous variables are presented as means ± standard deviation or as median and interquartile ranges where appropriate. The categorical variables are presented as percentages. The continuous variables were compared using the T-test or the Mann-Whitney U test as appropriate. Categorical variables were compared using the χ² test. Twelve-month mortality was analysed using the adjusted influence of CR on 12-month mortality. P values ≤ 0.1 were used in univariate analysis to introduce a variable into the multivariate analysis model. This included age, diabetes mellitus, chronic kidney disease, atrial fibrillation, the presence of severe mitral regurgitation, the presence of three vessel disease, chronic total occlusion (CTO), implantation of drug eluting stents, the presence of implanted cardioverter defibrillator, CR, the administration of beta-blockers, angiotensin converting enzyme inhibitors, statins, and mineralocorticoid receptor antagonists. The hazard ratios (HR) and 95% confidence intervals (CI) were calculated. A two-sided p-value ≤ 0.05 was considered significant. The STATISTICA 10 software (StatSoft, Inc., Tulsa, OK, USA) was used for all calculations.

**RESULTS**

Patient clinical characteristics, medical history, administered medical treatment, and echocardiographic parameters are presented in Table 1. No gender-based differences were observed. Patients in the CR group were younger and were more frequently post-PCI. In both groups, nearly a quarter of subjects were post-CABG. The CR patients had a significantly lower prevalence of diabetes (54.1% vs. 42.0%, p = 0.02) and chronic kidney disease stage III–V (33.9% vs. 23.4%, p = 0.04). There were no significant differences in baseline echocardiographic parameters (LVEF, ventricular dimensions, and volumes).

The angiographic and procedural characteristics are presented in Table 2. Patients with CR had a more favourable angiographic profile regarding the prevalence of three vessel disease and CTO. Drug eluting stents were implanted more frequently in CR patients, with no other significant differences between the study groups. The presence of CTO was the main reason for lack of CR (79.2%). Other reasons were: poor general clinical condition (11.9%), lack of PCI success (3.8%), confirmed lack of viability (3.1%), and confirmed lack of ischaemia in fractional flow reserve examination (1.9%). There were no differences regarding radiation exposure and the frequency of contrast-induced nephropathy.

The in-hospital and 12-month clinical outcome analysis is presented in Table 3. In-hospital MACCE comparison revealed no differences between the study groups. However, there was a significant difference in the 12-month all-cause mortality: 6.35% vs. 20.13% in favour of the CR group (p < 0.001; Fig. 2). Cox regression multivariate analysis of the complete study population confirmed that achievement of CR was an independent factor improving survival in the 12-month observation period (HR 0.39; 95% CI 0.18–0.81, p = 0.01; Fig. 3).

**DISCUSSION**

Coronary artery disease is the aetiological factor of two-thirds of all systolic HF cases, and its treatment poses a significant challenge [4]. Even though revascularisation has been shown to improve prognosis, data on specific therapeutic strategies is scarce and mostly related to CABG [5]. STICH remains the only contemporary randomised trial concerning the management of CAD in HF patients. Despite its results, reflected in the current myocardial revascularisation guidelines [6, 11], a large proportion of patients with HF and multi-vessel disease do not undergo CABG and are subsequently qualified for optimal medical treatment or PCI [7, 8, 12]. This was confirmed in our analysis, in which 47% of the initial population undergoing coronary angiography were qualified for subsequent percutaneous revascularisation, compared to only 10.6% qualified for CABG.

There are no randomised studies comparing PCI versus medical treatment or CABG in HF. The data on PCI in HF patients is mostly derived from large registries, concentrated predominantly on comparisons to CABG. However, in these studies, a strictly clinical definition of HF is utilised, with no significant left ventricular dysfunction confirmed by echocardiography. For instance, in a recently published analysis from the Credo-Kyoto registry on revascularisation in HF, the mean LVEF in the PCI arm was 46.6% [7], while in an analysis from the APPROACH registry, over 58% of revascularised patients had an LVEF of above 35% [12]. These data are difficult to extrapolate to the HF population with severely impaired LVEF.

With few studies on the role of PCI in ischaemic HF, information on particular strategies of intervention is even more limited. As there are no data on the completeness of revascularisation by PCI in patients with LVEF ≤ 35% and multi-vessel CAD, we decided to analyse the outcomes in a population in whom CR was achieved.

**Clinical characteristics**

Studies concerning revascularisation in HF, such as the STICH trial, consist mostly of patients of advanced age, with
a history of cardiovascular interventions and a large burden of comorbidities [5]. Similarly, the COMMIT-HF study group is characterised by substantial morbidity. The administration of guideline-based therapy is high. Although some baseline characteristic differences were observed among the study groups, they were proven not to significantly influence the primary outcome in multivariate analysis.

A comparison of the COMMIT-HF population to the STICH trial population reveals an older study group, notably more burdened with comorbidities and with higher New York Heart Association class, but with similar LVEF and administered medical therapy. In fact, the age and profile of comorbidities in the COMMIT-HF registry are more similar to those observed in studies strictly concerning high-risk PCI and haemodynamic support [13, 14]. Nonetheless, we consider the COMMIT-HF population to be representative of a real-life, contemporary ischaemic HF patient.

Table 1. Patient baseline characteristics, medical treatment, and echocardiographic parameters

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Total (n = 347)</th>
<th>CR (n = 188)</th>
<th>IR (n = 159)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years]</td>
<td>65.0 ± 10.9</td>
<td>63.7 ± 10.6</td>
<td>66.5 ± 11.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Female sex</td>
<td>17.2%</td>
<td>16.4%</td>
<td>18.2%</td>
<td>0.66%</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>27.8 ± 4.23</td>
<td>28.3 ± 4.2</td>
<td>27.3 ± 4.1</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Medical history and treatment

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 347)</th>
<th>CR (n = 188)</th>
<th>IR (n = 159)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD/CRT-D</td>
<td>52.4%</td>
<td>51.8%</td>
<td>53.4%</td>
<td>0.76</td>
</tr>
<tr>
<td>Anaemia</td>
<td>37.7%</td>
<td>37.7%</td>
<td>37.7%</td>
<td>0.99</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>47.5%</td>
<td>42.0%</td>
<td>54.1%</td>
<td>0.02</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>28.5%</td>
<td>23.9%</td>
<td>33.9%</td>
<td>0.04</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>24.7%</td>
<td>23.4%</td>
<td>26.4%</td>
<td>0.51</td>
</tr>
<tr>
<td>Prior myocardial infarct</td>
<td>74.3%</td>
<td>71.8%</td>
<td>77.3%</td>
<td>0.23</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>63.9%</td>
<td>76.6%</td>
<td>47.8%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>23.6%</td>
<td>24.6%</td>
<td>22.5%</td>
<td>0.68</td>
</tr>
<tr>
<td>NYHA III/IV</td>
<td>44.6%</td>
<td>40.9%</td>
<td>49.0%</td>
<td>0.13</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>94.2%</td>
<td>95.2%</td>
<td>93.8%</td>
<td>0.39</td>
</tr>
<tr>
<td>ACEI</td>
<td>74.8%</td>
<td>77.6%</td>
<td>71.5%</td>
<td>0.18</td>
</tr>
<tr>
<td>Diuretics</td>
<td>78.3%</td>
<td>78.7%</td>
<td>77.9%</td>
<td>0.94</td>
</tr>
<tr>
<td>Mineralocorticoid receptor antagonists</td>
<td>81.8%</td>
<td>84.0%</td>
<td>79.2%</td>
<td>0.24</td>
</tr>
<tr>
<td>(N)OAC</td>
<td>21.6%</td>
<td>23.4%</td>
<td>19.5%</td>
<td>0.37</td>
</tr>
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Echocardiographic parameters

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 347)</th>
<th>CR (n = 188)</th>
<th>IR (n = 159)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF [%]</td>
<td>27.9 ± 5.5</td>
<td>28.5 ± 5.6</td>
<td>27.3 ± 5.4</td>
<td>0.13</td>
</tr>
<tr>
<td>LVEDD [mm]</td>
<td>62.55 ± 7.9</td>
<td>62.5 ± 7.9</td>
<td>62.6 ± 7.8</td>
<td>0.86</td>
</tr>
<tr>
<td>LVESD [mm]</td>
<td>49.8 ± 9.4</td>
<td>49.4 ± 9.4</td>
<td>50.2 ± 9.2</td>
<td>0.46</td>
</tr>
<tr>
<td>LVEDV [mL]</td>
<td>187.5 ± 67</td>
<td>184.8 ± 66</td>
<td>190.7 ± 69</td>
<td>0.52</td>
</tr>
<tr>
<td>LVESV [mL]</td>
<td>140.8 ± 59</td>
<td>139.0 ± 61</td>
<td>142.9 ± 57</td>
<td>0.64</td>
</tr>
<tr>
<td>Severe MR</td>
<td>7.49%</td>
<td>6.38%</td>
<td>8.81%</td>
<td>0.39</td>
</tr>
</tbody>
</table>

*P value calculated for comparison of incomplete revascularisation (IR) vs. complete revascularisation (CR) groups; ACEI — angiotensin converting enzyme inhibitors; BMI — body mass index; CABG — coronary artery bypass grafting; CRT-D— cardiac resynchronisation therapy defibrillator; ICD — implanted cardioverter defibrillator; LVEDD — left ventricular end diastolic diameter; LVEDV — left ventricular end diastolic volume; LVEF — left ventricular ejection fraction; LVESD — left ventricular end systolic diameter; LVESV — left ventricular end systolic volume; MR — mitral regurgitation; NYHA — New York Heart Association; (N)OAC — (novel) oral anticoagulants; PCI — percutaneous coronary intervention.

Angiographic characteristics and procedure safety

The angiographic profile of patients with ischaemic HF is typically characterised by a high prevalence of multi-vessel disease, often with left main involvement or with CTOs, as presented in the STICH trial or the Credo-Kyoto registry [5, 7]. In studies concerning the completeness of revascularisation, the angiographic profile is usually more favourable in the CR group [9, 15–17]. Accordingly, the angiographic characteristics in the COMMIT-HF population were comparable to those presented in the aforementioned studies, with a favourable angiographic profile in the CR group. This was caused mostly by a higher prevalence of CTO. Its presence in clinical practice is the most important cause for the lack of CR. PCI of CTO is still not a routine procedure, even in patients with preserved left ventricular function. Less than 10% of CTO patients are qualified for percutaneous revascularisation [18]. The cur-
The frequency of recanalisation in our study was comparable to that reported in patients with stable CAD. Despite a lack of clear guidelines, it seems that ischaemic HF patients may benefit even more from CTO revascularisation.
Data on PCI safety in ischaemic HF patients is lacking. In our analysis, procedural safety was satisfactory in both study groups. Despite a substantial burden of chronic kidney disease and diabetes, the frequency of contrast-induced nephropathy was low, with none of the patients requiring renal-replacement therapy. Radiation exposure was at an acceptable level. The occurrence of in-hospital MACCE was low and similar in both study groups. The PCI characteristics were comparable as well, with a large percentage of procedural success in both groups. These data clearly support the safety and feasibility of PCI in ischaemic HF patients.

Completeness of revascularisation

Completeness of revascularisation remains one of the unanswered questions in patients with preserved LVEF. Despite being under investigation for over 20 years, there are still major doubts in this area, reaching as far as the lack of a unified definition of CR. In patients with HF there are additional factors determining the haemodynamics of coronary blood flow. Restoration of perfusion in regions of hibernated myocardium in this population may lead to improved contractility and minimised adverse ventricular remodelling, which should have a much more prominent effect relative to patients with
preserved ejection fraction. The influence on the occurrence of ventricular arrhythmia may also be of utmost importance. Despite a lack of evidence of arrhythmic substrate modification with coronary revascularisation [22], ischaemia — even in nonviable myocardium territory — can be considered a potential arrhythmia trigger.

With these data under consideration, we have selected the anatomical definition of CR for this analysis. Our analysis shows that angiographic completeness of revascularisation is feasible, with over half of patients achieving this treatment goal.

**Long-term outcomes**

Data on CR achieved by both CABG and PCI have been somewhat ambiguous, but there is a general trend that CR improves outcomes [15–17, 23, 24]. However, in these studies, patients with impaired left ventricular function were either excluded from analysis or represented a marginal proportion of subjects. To the best of our knowledge, the only study to demonstrate the benefit of CR in patients with impaired LVEF was the analysis by Bell et al. [9] from the CASS registry, published in 1990.

The overall 12-month mortality rate in the COMMIT-HF patients undergoing PCI was comparable to that presented in the CABG arm of the STICH trial. However, in our population there was a significant survival benefit in the CR group. Despite favourable clinical and angiographic characteristics, the results of the Cox regression analysis identified achievement of CR in ischaemic HF patients with multi-vessel CAD as an independent factor improving 12-month survival. Such differences were not observed in previous studies concerning CR in patients with preserved LVEF. This may be due to an even larger impact of CR in patients with ischaemic HF. In this group CR potentially leads to less recurrent ischaemia, preservation of left ventricular function, reduced rate of myocardial infarctions, ventricular arrhythmias, and potentially better tolerance of subsequent ischaemic events.

The results of our analysis underline the impact that achievement of CR has on improvement of prognosis in ischaemic HF patients. Many factors, such as the presence of CTO, may hamper efforts to achieve this treatment target. With this under consideration, the qualification of a patient with ischaemic HF and multi-vessel disease for PCI rather than CABG should be considered when complete revascularisation as a final treatment goal is possible. Nonetheless, while CR after PCI is desirable and feasible, patient safety should always be a priority. If CR is considered impossible, a reasonable incomplete revascularisation can also be a satisfactory option.

**Limitations of the study**

There are several limitations of our analysis. The retrospective analysis of PCI results, differences in baseline characteristics, as well as the decision to implement the anatomical definition of CR are all potential weaknesses. The main angiographic limitation of our analysis was the large proportion of patients with CTO in the incomplete revascularisation group. This indicates that patients qualified for CR formed a group in which CR was technically feasible. Differences in baseline comorbidity profile were also observed. Despite the inclusion of all available patient data in the COMMIT-HF registry, even after adjusting for confounding factors, the results may be biased by potential important, unidentified, and unforeseeable factors not available in the registry. The conclusions of our analysis require confirmation in a randomised trial.

**CONCLUSIONS**

Analysis of the COMMIT-HF population suggests that feasibility and achievement of complete revascularisation may improve survival in this difficult patient population. Moreover, we have demonstrated that PCI can be a safe and effective method of revascularisation in ischaemic heart failure.

**Conflict of interest: none declared**

**References**


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Kompletna przeszkórnna rewaskularyzacja w niedokrwiennej niewydolności serca poprawia rokowanie: wnioski z rejestru COMMIT-HF

Łukasz Pyka, Michał Hawranek, Mateusz Tajstra, Jarosław Gorol, Andrzej Lekston, Mariusz Gąsior

III Katedra i Oddział Kliniczny Kardiologii, Wydział Lekarski z Oddziałem Lekarsko-Dentystycznym w Zabrzu, Śląski Uniwersytet Medyczny, Katowice

Streszczenia

Wstęp i cel: Niewydolność serca (HF) stanowi podstawową przyczynę zgonu wśród pacjentów z chorobami sercowo-naczyniowymi. Po badaniu STICH nadal brakuje danych dotyczących roli angioplastyki wieńcowej (PCI) w skurczowej niedokrwiennej HF. Rola kompletności rewaskularyzacji pozostaje niejasna.

Metody: COMMIT-HF to aktualnie prowadzony rejestr skurczowej HF (frakcja wyrzutowa lewej komory ≤ 35% przy wystąpieniu ostrych zespołów wieńcowych). Dotychczas do badania włączono 1798 pacjentów. Z rejestru wyselekcjonowano osoby z wielonaczyniową postacią choroby wieńcowej zakwalifikowane do PCI, a następnie podzielono na grupę kompletną (n = 188) i niekompletną (n = 159) rewaskularyzacji. Kompletność rewaskularyzacji definiowano jako skuteczną PCI wszystkich istotnych zmian w tętnicach o średnicy ≥ 2 mm bez działającego pomostu. Pierwszorzędowy punkt końcowy stanowiła 12-miesięczna śmiertelność ze wszystkich przyczyn.

Wyniki: Pomiędzy grupami nie stwierdzono istotnych różnic pod względem parametrów echokardiograficznych, przy niższej częstości chorób współistniejących w grupie kompletnej rewaskularyzacji. Parametry okołozabiegowe były porównywalne. Nie stwierdzono istotnych różnic w zakresie powikłań. Śmiertelność ze wszystkich przyczyn była istotnie niższa w grupie kompletnej rewaskularyzacji (6,4% vs. 20,1%; p < 0,001). Analiza wieloczynnikowa potwierdziła, że uzyskanie kompletnej rewaskularyzacji stanowiło niezależny czynnik poprawiający rokowanie (HR 0,39; 95% CI 0,18–0,81; p = 0,01).

Wnioski: Przeszkórna interwencja wieńcowa może być bezpieczną i skuteczną metodą rewaskularyzacji w HF. Uzyskanie kompletnej rewaskularyzacji w populacji pacjentów objętych niniejszym badaniem wiązało się z istotnie lepszym rokowaniem.

Słowa kluczowe: przeszkórna angioplastyka wieńcowa, niewydolność serca, choroba wieńcowa

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