Left main coronary disease: improved early outcomes after off-pump coronary artery bypass grafting in high-risk patients

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Abstract

Background: Left main coronary artery (LMCA) stenosis is a risk factor in coronary artery bypass grafting (CABG). Although improved outcomes of off-pump CABG have been well documented, LMCA stenosis is often perceived as a contraindication for off-pump CABG. In this study, we compared on-pump and off-pump techniques in high-risk patients with LMCA disease.

Aim: Documentation of safety and feasibility of off-pump CABG in patients with LMCA disease.

Methods: One hundred ninety nine patients with LMCA disease and a EuroScore ≥ 5 were operated upon between 2007 and 2010. One hundred patients (Group I) were operated upon using off-pump techniques, while 99 (Group II) were operated upon using conventional on-pump techniques. Perioperative variables and outcomes at first six months were compared.

Results: Despite higher mean age and EuroScore (70.9 ± 4.8 vs. 65.6 ± 7.9, p < 0.001, and 6.09 ± 0.8 vs. 5.31 ± 0.68, p < 0.001, respectively), and lower ejection fraction (41.4 ± 7.3 vs. 49.0 ± 6.2, p < 0.001), hospital mortality (1% vs. 6.1%, p = 0.065), postoperative inotropic support (9% vs. 48.4%, p < 0.001), blood loss (680.6 ± 265.0 vs. 847.2 ± 382, p < 0.001) and transfusions of blood (0.57 ± 0.79 U vs. 1.49 ± 0.82 U, p < 0.001), and hospital stay (6.57 ± 2.04 vs. 7.68 ± 3.44, p = 0.006) were lower in Group I. In both groups, mean number of distal anastomoses and completeness of revascularisation were similar.

Conclusions: Using the off-pump technique is safe and improves postoperative early outcomes in high-risk patients with LMCA disease.

Key words: off-pump surgery, coronary artery bypass surgery, outcomes

INTRODUCTION

Left main coronary artery (LMCA) disease is recognised as a risk factor for cardiac related adverse events [1], and the prognostic benefits of surgical intervention over medical therapy are well documented [2]. The presence of LMCA stenosis has been accepted as a risk factor in patients undergoing coronary artery bypass grafting (CABG) surgery both in early [3] and late phases [4]. Although coronary revascularisation using cardiopulmonary bypass (CPB) remains the gold standard treatment for coronary artery disease [5], CPB has many undesirable effects with a potential to affect the postoperative outcomes in a high-risk population [6], and the use of off-pump techniques during CABG surgery has been shown to improve early outcomes significantly [7].

However, due to concerns about the heart’s ability to tolerate, cardiac surgeons have been traditionally reluctant to use off-pump techniques in patients with LMCA stenosis. Although recently published studies have documented the safety and success of off-pump CABG in LMCA stenosis [8–11], data comparing both techniques in high-risk LMCA patients is limited.
Therefore this study was intended to compare early and midterm results of both on-pump and off-pump techniques in high-risk LMCA disease patients.

METHODS
Patient population
This study was conducted retrospectively in a cohort of 199 high-risk patients with critical LMCA disease who were operated upon between 2006 and 2010. One hundred of this patient group were operated upon without CPB support and constituted Group I, whereas Group II comprised 99 patients who were operated upon under CPB with moderate hypothermia and cardioplegic cardiac arrest conditions. All patients in both groups were operated upon by the same surgeons (UK, MK and GO) and the decision as to whether to use CPB was made by the individual surgeon according to the patient’s risk status in a nonrandomised manner on the basis of medical comorbidities that were believed to increase the risk of CPB. Patients with comorbid conditions and without significant risk factors were not included in the study. Patients were stratified as high-risk candidates in the presence of a EuroScore ≥ 5. This study was approved by Diskapi Y. B. E. A. Hospital Ethics Committee on 10 January, 2011.

Clinical data collection, monitoring and definitions
Outcomes of the first six postoperative months were recorded. Follow-up was achieved by direct communication with the patient, the patient’s family, or the attending physician. All the patients had echocardiography in the sixth postoperative month. Critical LMCA disease was defined as stenosis of LMCA equal to or more than 50% in accordance with The Society of Thoracic Surgeons’ database. Operative mortality was defined as any death that occurred within 30 days of the operation. Postoperative stroke was defined as a new neurologic event persisting for more than 24 hours after onset and was confirmed by computed tomography or magnetic resonance imaging, whereas a transient ischaemic attack (TIA) was defined if the deficit resolved within 24 hours. Postoperative inotropic support was defined as infusions of any inotropic medication other than 3 µg/kg/min dopamine infusion. Postoperative renal failure was defined as the requirement for haemodialysis. Perioperative myocardial infarction was considered if there was documentation of new abnormal Q waves and elevated cardiac enzymes (creatine kinase-myocardial band, CK-MB > 50 U/L and cardiac troponin I > 12 ng/mL).

Anaesthesia and anticoagulation
A standard anaesthetic technique was used for all patients. The induction of anaesthesia was achieved with fentanyl citrate (5 to 10 µg/kg), thiopental (3 to 5 mg/kg), or propofol infusion (3 to 4 mg/kg/h), and vecuronium bromide (0.1 mg/kg). Anaesthesia was maintained with fentanyl, propofol (2 to 3 mg/kg), and low concentrations of sevoflurane as necessary. Standard intraoperative monitoring techniques were used.

All off-pump patients received 5,000 U heparin as a standard dose during internal thoracic artery harvest, while the same dose was repeated when overt coagulation was seen on the operative field.

In Group II, CPB was commenced after standard aortic-right atrial cannulation with a mild hypothermia between 32–34°C and a nonpulsatile flow of 2.4 L/min per square metre of body surface area. Membrane oxygenators and roller pump heads were used for CPB. Cardiac arrest was achieved with antegrade cold crystalloid cardioplegic solution (Plegisol, Hospira Inc., Lake Forest, IL, USA) induction and intermittent antegrade or retrograde blood cardioplegic maintenance every 20 min.

In both groups, all distal anastomoses were performed with 8–0 polypropylene sutures, whereas 7–0 and 6–0 sutures were used for proximal anastomoses of arterial and venous grafts respectively. In all patients, their left anterior descending artery (LAD) and at least one obtuse marginal artery were grafted regardless of the degree of stenosis, while other vessels with lesions equal to or more than 70% stenosis received grafts. Sequential anastomose techniques were used selectively according to coronary anatomy and the individual surgeon’s preference. In off-pump patients, LAD artery was anastomosed first, while in on-pump patients the most critically stenosed vessel was grafted first and LAD was the last vessel to be grafted. In off-pump patients, systolic blood pressure was kept between 50–60 mm Hg and heart rate was decreased to 50–60 bpm. Beta-blocker agents, Trendelenburg positioning and cristalloid volume replacements were used as needed according to the haemodynamics of individual patients. None of the patients in the off-pump group received inotropic agents during the stabilisation. None of the patients in the off-pump group had decompenation. Only one patient...
was converted to CPB due to inadvertent injury of a fragile coronary sinus; consequently the operation was completed in beating heart on CPB conditions.

Statistical analysis
Discrete variables are displayed as proportions, continuous variables as mean ± standard deviation unless specified otherwise. The \( \chi^2 \) or Fisher’s exact test was used to analyse the categorical data. Differences between continuous variables were analysed using one-way analysis of variance. A probability value of less than 0.05 was considered significant. Statistical analyses were performed with SPSS 15.0 for Windows (SPSS, Chicago, IL, USA).

RESULTS
Preoperative clinical data of study groups is summarised in Table 1. Mean age and EuroScore was significantly higher in Group I than Group II (70.9 ± 4.8 vs. 65.6 ± 7.9, \( p < 0.001 \), and 6.09 ± 0.8 vs. 5.31 ± 0.68, \( p < 0.001 \), respectively), whereas preoperative mean left ventricle ejection fraction (LVEF) was significantly lower in off-pump patients (41.4 ± 7.3 vs. 49.0 ± 6.2, \( p < 0.001 \)). Although variables like chronic obstructive pulmonary disease (COPD), peripheral vascular disease, renal failure, congestive heart failure (CHF), recent myocardial infarction (MI) and emergent surgery were more prevalent in Group I, the differences did not reach statistical significance. The rest of the preoperative clinical data was similar.

Perioperative data is set out in Table 2. Although hospital mortality was lower in Group I (1% vs. 6.1%, \( p = 0.065 \)), this failed to reach statistical significance. The single death in Group I was attributable to respiratory failure in a patient with severe COPD, while the most frequent mode of death was low cardiac output in Group II patients. In both groups, the mean numbers of distal anastomoses and completeness of revascularisations were similar (3.37 ± 0.7 in Group I vs. 3.39 ± 0.7 in Group II, \( p = 0.81 \) and 95% in Group I vs. 96% in Group II, \( p = 0.50 \), respectively). Postoperative inotropic support (9% vs. 48.4%, \( p < 0.001 \)), blood loss (680.6 ± 265.0 vs. 847.2 ± 382, \( p < 0.001 \)) and transfusions of blood (0.57 ± 0.79 U vs. 1.49 ± 0.82 U, \( p < 0.001 \)) and fresh frozen plasma (2.54 ± 1.82 U vs. 4.42 ± 2.5 U, \( p < 0.001 \)), intraoperative defibrillation (3% vs. 19%, \( p < 0.001 \)), postoperative pacing requirement (2% vs. 9.1%, \( p < 0.03 \)) and hospital stay (6.57 ± 2.04 days vs. 7.68 ± 3.44 days, \( p = 0.006 \)) were significantly lower in patients operated upon using the off-pump technique. Both groups were comparable in variables like bilateral internal thoracic artery and radial artery use, perioperative MI and superficial and deep sternal infections. Only one patient in Group I had conversion to CPB due to inadvertent coronary sinus injury. Perioperative variables like postoperative ventilation time, re-operation for bleeding/tamponade, postoperative intraaortic balloon pump (IABP) use, postoperative atrial fibrillation, postoperative TIA and stroke and renal failure frequencies were lower in Group I, but without statistical significance (Table 2). At the six month follow-up, one patient in Group I and three patients in Group II had died due to CHF. None of the patients in either groups required either repeat angiography or revascularisation. The occurrences of CHF over the long term were less in Group I, without statistical significance (8% vs. 17.2%, \( p = 0.08 \)). Correlated to preoperative values, late postoperative LVEF values too were significantly lower in Group I compared to Group II (Fig. 1). In Group II, mean LVEF were lower in the late postoperative period compared to preoperative levels (45 ± 5.2 vs. 49 ± 6.2, \( p = 0.04 \)), while the same variable did not change in Group I after operation (41.4 ± 7.3 vs. 41.6 ± 6.0, \( p = 0.83 \)).

DISCUSSION
The detrimental effects of CPB and myocardial ischaemia of cardioplegic cardiac arrest have been well demonstrated. In addition to systemic effects like volume retention, coagulopathy, release of systemic inflammatory mediators, pulmonary dysfunction, stroke and neurocognitive changes [6], CPB also causes cardiac effects like subendocardial underperfusion.
and deteriorated interventricular septal function [14] in patients with coronary artery disease. In addition to being free of the undesired effects of CPB, better preserved myocardial metabolism [15], significantly less myocardial ischaemia [16] and an improvement in left ventricular functions have been shown with off-pump CABG [17]. Correlated to these findings, the introduction of off-pump techniques in CABG surgery improved both early and late clinical outcomes [5] and allowed higher risk patients to be operated upon with even better outcomes compared to relatively lower risk patients operated upon with CPB [18]. Since these techniques involve rigorous displacement of the heart, and low cardiac output, many surgeons have been concerned about the risk of decompensation in LMCA disease [9].

Therefore LMCA disease has been assumed to be a contraindication to off-pump surgery, which precluded widespread use of this technique in these high-risk patients. Despite this belief, several studies have documented the benefits of off-pump CABG in LMCA disease [10, 11]. However, studies comparing the off-pump technique to the on-pump technique in high-risk patients with LMCA disease are scarce. Since the beneficial effects of the off-pump technique are most evident in high-risk patients [19], we preferred to include only high-risk patients in our study group.

It is worth noting that in our series, individual surgeons have tended to use the off-pump technique in high-risk patients as documented by the higher frequency of risk factors such as left ventricular dysfunction, older age and higher EuroScore

Table 2. Perioperative data

<table>
<thead>
<tr>
<th></th>
<th>Off-pump (n = 100)</th>
<th>On-pump (n = 99)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital mortality</td>
<td>1 (1%)</td>
<td>6 (6.1%)</td>
<td>0.065</td>
</tr>
<tr>
<td>No. distal anastomoses</td>
<td>3.37 ± 0.7</td>
<td>3.39 ± 0.7</td>
<td>0.82</td>
</tr>
<tr>
<td>XCI time</td>
<td>N/A</td>
<td>51 ± 11.3</td>
<td>N/A</td>
</tr>
<tr>
<td>CPB time</td>
<td>N/A</td>
<td>72.1 ± 14.5</td>
<td>N/A</td>
</tr>
<tr>
<td>Complete revascularisation</td>
<td>95 (95%)</td>
<td>95 (96%)</td>
<td>1.00</td>
</tr>
<tr>
<td>BITA use</td>
<td>14 (14%)</td>
<td>17 (17.2%)</td>
<td>0.67</td>
</tr>
<tr>
<td>RA use</td>
<td>33 (33%)</td>
<td>32 (32.2%)</td>
<td>0.91</td>
</tr>
<tr>
<td>Defibrillation</td>
<td>3 (3%)</td>
<td>19 (19.2%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Conversion to CPB</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Total blood loss [mL]</td>
<td>680.6 ± 265.9</td>
<td>847.2 ± 382.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Transfused blood [U]</td>
<td>0.57 ± 0.79</td>
<td>1.49 ± 0.82</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Transfused fresh frozen plasma [U]</td>
<td>2.54 ± 1.82</td>
<td>4.42 ± 2.50</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Ventilation time [h]</td>
<td>14.5 ± 24.4</td>
<td>20.2 ± 30.9</td>
<td>0.15</td>
</tr>
<tr>
<td>Re-operation for bleeding/tamponade</td>
<td>3 (3%)</td>
<td>7 (7.1%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Postoperative pacing requirement</td>
<td>2 (2%)</td>
<td>9 (9.1%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Postoperative isotropic support</td>
<td>9 (6%)</td>
<td>48 (48.4%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IABP</td>
<td>3 (3%)</td>
<td>10 (10.1%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Perioperative MI</td>
<td>1 (1%)</td>
<td>2 (2%)</td>
<td>0.90</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>15 (15%)</td>
<td>24 (24.2%)</td>
<td>0.14</td>
</tr>
<tr>
<td>TIA</td>
<td>3 (3%)</td>
<td>8 (8.1%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Postoperative stroke</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Postoperative renal failure</td>
<td>1 (1%)</td>
<td>4 (4%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Superficial sternal infection</td>
<td>5 (5%)</td>
<td>3 (3%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Deep sternal infection</td>
<td>2 (2%)</td>
<td>1 (1%)</td>
<td>0.50</td>
</tr>
<tr>
<td>ICU stay [days]</td>
<td>2.04 ± 1.1</td>
<td>2.22 ± 1.4</td>
<td>0.323</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>6.57 ± 2.04</td>
<td>7.68 ± 3.44</td>
<td>0.006</td>
</tr>
<tr>
<td>Late LVEF</td>
<td>41.6 ± 6.0</td>
<td>45.0 ± 5.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Late congestive heart failure</td>
<td>8 (8%)</td>
<td>17 (17.2%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Late mortality</td>
<td>1</td>
<td>3</td>
<td>0.35</td>
</tr>
</tbody>
</table>

XCI — cross clamp; CPB — cardiopulmonary bypass; BITA — bilateral internal thoracic arteries; RA — radial artery; IABP — intraaortic balloon pump support commenced at perioperative period only; Perioperative MI — perioperative myocardial infarction; TIA — transient ischaemic attack; Late LVEF — left ventricle ejection fraction in sixth postoperative month; ICU — intensive care unit; N/A — not applicable
in Group I, and have tended to reserve CPB for patients with lower risk. Additionally, factors like COPD, peripheral vascular disease, renal failure, CHF, recent MI and emergent surgery have been slightly more prevalent in off-pump patients.

Despite this selection bias against Group I, patients operated upon with the off-pump technique had better outcomes as evidenced by significantly lesser need for postoperative inotropic support, pacing and intraoperative defibrillation and shorter hospital stay. Likewise, Group I also had significantly less postoperative blood loss and transfusions of blood and fresh frozen plasma compared to Group II. Mortality in on-pump patients was higher than in the off-pump group and the difference is only just insignificant, something which is attributable to the small number of study groups. The much higher incidence of low cardiac output in Group II compared to Group I is also remarkable. Similarly, even though statistically insignificant, we noted shorter ventilation time, and lower frequency of re-operation, IABP usage, development of atrial fibrillation, TIA, stroke and renal failure in Group I.

An important concern in patients undergoing off-pump surgery is incomplete revascularisation. In Yeatman’s report, improved outcomes in off-pump CABG have been achieved at the cost of a less complete revascularisation [8]. Significantly fewer used grafts in off-pump patients has also been reported by Virani et al. [20], who concluded that LMCA disease should no longer be seen as a contraindication to perform off-pump CABG. Unlike their experience, Emmert et al. [11] compared LMCA and non-LMCA patients operated upon with the off-pump technique and achieved almost complete revascularisation in both groups.

Our results clearly demonstrate that improved outcomes in off-pump CABG, even in high-risk patients, do not come at the cost of an incomplete revascularisation (95% in Group I vs. 96% in Group II, p = 0.50) which is a bad long term outcome predictor.

Although the relative discrepancy of better results in higher risk patients in the off-pump group compared to the on-pump group is notable, we believe this finding is in agreement with the results of experts in this technique who have found that the higher the risk of patients, the greater the benefit of off-pump CABG [19, 21].

Another point of interest could be the incongruity of our results with two published randomised trials: ROOBY [22] and CORONARY [23]. Neither trial showed the benefit of off-pump CABG in predominantly non-LMCA patients (patients with critical LMCA disease was only 24% and 22%, respectively). The ROOBY trial has been criticised for shortcomings such as the lower risk of patients (EuroScore 2.5 vs. 6.09 in our off-pump group) and the inclusion of surgeons less experienced in the off-pump technique. Similarly, the CORONARY trial also has a different set of patients as a whole group compared to our study, as evidenced by a mean EuroScore of 3.8. Recently, a subgroup analysis of the CORONARY study has documented an important benefit of the off-pump technique in high risk patients in patients with a EuroScore of 3–5 and > 5 [personal communication with Dr. Lamy]. We believe our study cannot be compared to the ROOBY trial, whereas, when similar patients were compared, our results are congruous with the CORONARY trial.

Our revascularisation strategy includes revascularisation of the LAD area first to ensure the protection of myocardial perfusion and function during revascularisation of relatively haemodynamically challenging circumflex area. In our experience, the use of vacuum stabilisers and intracoronary shunts should be avoided in order to obtain more tolerant and improved haemodynamics and to protect the endothelium which is of the utmost importance, respectively. Similarly, CO₂ insufflation for clarity of the anastomose area was not come at the cost of an incomplete revascularisation (95% in Group I vs. 96% in Group II, p = 0.50) which is a bad long term outcome predictor.

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**Limitations of the study**

We believe the absence of randomisation and selection bias leading to higher risk patients being operated upon using the off-pump technique are the major limitations of this study. With randomisation, insignificant differences of parameters would be significant. However, we could not dare to put very high-risk patients with several comorbidities on CPB. For this reason, in our opinion our results reflect a real-world experience. The relatively small sample size is another limiting factor preventing the differences of several perioperative parameters from reaching statistical significance. One further
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limitation to the present study is the absence of late outcomes and long term patency data; we consider these to be subjects for a future study.

**CONCLUSIONS**

We believe the off-pump CABG technique is safe and offers better early and intermediate outcomes in a high-risk patient group with LMCA disease compared to those obtained by conventional CABG.

It should be preferred in high-risk patients and it allows us to give a chance of CABG to otherwise near inoperable patients. Further refinements of the technique such as complete arterial revascularisation and the avoidance of aortic manipulation would further improve early and late outcomes.

**Conflict of interest:** none declared

**References**

Choroba pnia lewej tętnicy wieńcowej: poprawa wczesnych wyników leczenia po pomostowaniu tętnic wieńcowych bez użycia krążenia pozaustrojowego u pacjentów z grupy wysokiego ryzyka

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Streszczenie

Wstęp: Zwężenie pnia lewej tętnicy wieńcowej (LMCA) jest czynnikiem ryzyka w przypadku pomostowania tętnic wieńcowych (CABG). Mimo że istnieje wiele danych potwierdzających, iż zabiegi CABG bez użycia krążenia pozaustrojowego (off-pomp CABG) wiążą się z lepszymi wynikami leczenia, zwężenie LMCA jest często uważane za przeciwwskazanie do wykonania tego zabiegu. W niniejszym badaniu porównano CABG z zastosowaniem krążenia pozaustrojowego i bez użycia krążenia pozaustrojowego u pacjentów z chorobą LMCA.

Cel: Celem badania było udowodnienie, że zabieg CABG bez krążenia pozaustrojowego jest bezpieczny i możliwy do wykonania u pacjentów z chorobą LMCA.

Metody: Do badania włączono 199 osób z chorobą LMCA z punktacją EuroScore ≥ 5, operowanych w latach 2007–2010. U 100 pacjentów (grupa I) przeprowadzono zabieg bez użycia krążenia pozaustrojowego, natomiast u 99 (grupa II) zastosowano konwencjonalną metodę z krążeniem pozaustrojowym. Porównano zmienne okołooperacyjne i wyniki leczenia w ciągu 6 miesięcy po zabiegu.

Wyniki: Mimo wyższych średnich wieku i punktacji EuroScore (odpowiednio 70,9 ± 4,8 vs. 65,6 ± 7,9; p < 0,001 i 6,09 ± 0,8 vs. 5,31 ± 0,68; p < 0,001) oraz mniejszej frakcji wyrzutowej (41,4 ± 7,3 vs. 49,0 ± 6,2; p < 0,001) w grupie I śmiertelność wewnątrzszpitalna (1% vs. 6,1%; p = 0,065), odsetek pacjentów wymagających podawania leków inotropowych (9% vs. 48,4%; p < 0,001), utrata krwi (680,6 ± 265,0 vs. 847,2 ± 382; p < 0,001) i ilość przetoczonej krwi (0,57 ± 0,79 j. vs. 1,49 ± 0,82 j.; p < 0,001) były mniejsze, a czas pobytu w szpitalu krótszy (6,57 ± 2,04 vs. 7,67 ± 3,44; p = 0,006). W obu grupach średnia liczba zespołów dystalnych i odsetek całkowitych rewaskularyzacji były podobne.

Wnioski: Stosowanie metody off-pump (bez użycia krążenia pozaustrojowego) jest bezpieczne i wiąże się z poprawą wyników leczenia we wczesnym okresie pooperacyjnym u pacjentów z grupy wysokiego ryzyka z chorobą LMCA.

Słowa kluczowe: zabieg bez użycia krążenia pozaustrojowego, pomostowanie aortalno-wieńcowe, wyniki leczenia

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