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Cardiac venous arterialization in acute myocardial infarction: how great is the benefit?

Maria Munz[a,*†], Mário J. Amorim[b,c,†], Miguel Faria[a], Corália Vicente[a], Ana Pinto[a], Joana Monteiro[a], Adelino F. Leite-Moreira[b,c] and Artur P. Águas[a]

[a] ICBAS (Abel Salazar Institute for Biomedical Sciences), University of Porto, Porto, Portugal
[b] Department of Physiology and Cardiothoracic Surgery, Faculty of Medicine, University of Porto, Porto, Portugal
[c] Department of Cardiothoracic Surgery, Centro Hospitalar São João, EPE, Porto, Portugal

* Corresponding author. Departamento de Anatomia, Instituto de Ciências Biomédicas de Abel Salazar, Rua de Jorge Viterbo Ferreira 228, 4050-313 Porto, Portugal. Tel: +35-12-20428101; fax: +35-12-22062232; e-mail: mariarod@icbas.up.pt (M. Munz).

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Abstract

OBJECTIVES: Cardiac venous arterialization has been proposed as an alternative approach for myocardial revascularization in ischaemic heart disease. It is based on using the cardiac venous system to transport arterial blood from a systemic artery to infarcted myocardial areas. Our goal was to evaluate its benefit in reducing acute myocardial infarct size and its effects on cardiac performance.

METHODS: In a group of pigs, the left internal mammary artery was anastomosed to the left anterior descending vein; this vein was ligated proximally. The left anterior descending coronary artery was also occluded. Over 5 days, several diagnostic procedures were used to characterize and measure the extent of myocardial infarct, namely ECG, echocardiography, cardiac biomarkers and histopathology. Data were compared with those from a control group of pigs, which were submitted to ligation of only the left anterior descending coronary artery.

RESULTS: In the experimental group, echocardiography revealed that the ejection fraction and thickness of the ventricular walls remained unchanged 4 days after surgery, in contrast to the major alterations in the control group. In fact, the ejection fraction in the control group decreased by 21% ($P < 0.001$), with a reduction of 31% ($P < 0.004$) in the thickness of the interventricular septum at end systole and enlargement of the left ventricular lumen by 28% ($P < 0.001$). In the experimental group, the sum for ST segment shift was 50% lower ($P = 0.038$) and the total ventricular histological lesion size was 50% smaller ($P < 0.001$). Within this lesion, the area of necrotic tissue was 70% smaller ($P < 0.001$). Cardiac biomarkers were not different between the two groups ($P > 0.2$).

CONCLUSIONS: This study reveals that selective cardiac venous arterialization can nourish the myocardium and is able to reduce infarct size by more than 50%, while protecting cardiac performance. We believe, therefore, that further investigation should be carried out into this technique in order for it to be considered as an option in coronary surgery.

Keywords: Cardiac veins • Arterialization • Retroperfusion • Myocardial infarction • Pig

INTRODUCTION

Ischaemic cardiomyopathy is a major cause of death in developed countries, with myocardial infarction (MI) being its most common and deadliest form. When the disease is due to focal and proximal narrowing of epicardial coronary arteries, coronary artery bypass grafting or percutaneous coronary interventions, such as angioplasty (with or without stents), are often successful therapeutic strategies. Unfortunately, atherosclerosis continues to progress, and the frequency of coronary restenosis is still high. Besides, neither of these techniques can be applied to patients with widespread coronary lesions [1, 2]. For these patients, a potential therapeutical approach would be to use their cardiac venous vasculature to transport arterial blood to the myocardium. Other interesting approaches, such as transmyocardial laser revascularization and regenerative therapies (using stem cells or genes), are also under investigation and have been used in clinical trials, mainly as adjunctive therapies in coronary artery bypass grafting. However, besides the risks involved, these techniques require optimization, and larger scale studies need to be performed for clear demonstration of efficacy and safety [3–5].

In the present experimental investigation, we have revisited the usefulness of revascularization of infarcted areas through cardiac venous arterialization. We used two groups of pigs. The control group was submitted to ligation at only the middle point of the left anterior descending coronary artery (LAD), in order to induce focal MI close to the apex of the heart. These animals were used as a control group. Using the same area at risk, the

[†] Both authors have contributed equally to this study.

experimental group was submitted to both mid-LAD ligation and cardiac venous arterialization, by grafting the left internal mammary artery (LIMA) to the left anterior descending coronary vein (LADV). This graft allowed the arterial blood coming from the LIMA to flow in a retrograde direction through the cardiac venous system, thereby reaching the myocardial capillaries. Additionally, the LADV was ligated proximally to the established shunt to avoid backflow into the coronary sinus, thus improving the blood flow towards the myocardial capillaries. Pigs from both groups were followed up for 5 days, and several parameters were evaluated before and after the surgical procedure, namely cardiac biochemical markers, ECGs and echocardiograms. After the pigs were killed, hearts were collected and analysed histologically to quantify necrotic lesions and granulation tissue. Through comparison of cardiac data between the two groups, it was possible to determine to what extent the arterialized LADV can rescue/prevent infarcted myocardial lesions.

With this research, and through the use of modern diagnostic equipment, it is our goal to contribute more accurate information regarding the efficacy of cardiac venous arterialization in reaching inaccessible ischaemic myocardial areas and its ability to preserve cardiac performance. As an ultimate goal, we expect this technique to reduce the mortality and morbidity of patients with ischaemic coronary disease, at least for those patients considered inoperable by other revascularization methods, who represent 12–15% of the total number of candidates [2].

MATERIALS AND METHODS

We used 26 healthy male pigs, of Landrace mixed breed, 3 months old and weighing between 34 and 40 kg. All experiments were conducted according to the European Union Directive no. 86/609/CEE for the use of animals in research.

For the control group, MI was induced in 13 pigs by surgical ligation at the middle point of the LAD. Detailed information about this model was previously published elsewhere [6]. The described anaesthetic protocol, intraoperative and postoperative care were performed identically in both groups (control and experimental).

In the experimental group, 13 pigs underwent mid-LAD ligation and cardiac venous arterialization. After partial sternotomy (the manubrium was spared), a sternal retractor (GeoMed® LA 330-00, Tuttlingen, Germany) was used to provide full exposure of the LIMA and the left surface of the heart. The LIMA was carefully dissected and released throughout the whole length of the sternum, by use of an electric scalpel (Diatermo®; Top-Sharp International Enterprise, Hong Kong, China) and by double clipping its secondary branches (small SLS™ clips; MoonSurge, Lisbon, Portugal). The distal end of the LIMA was secured with a clamp and transected, in order to tunnel it through the pericardium to reach the LADV. The LADV was then prepared for anastomosiis with the LIMA. For this purpose, by use of a cardiac stabilizer (Medtronic® Octopus; International Trading, Sàrl Tolochenaz, Switzerland), a small cut 2 mm in length was performed on the LADV to permit intraluminal introduction of a 2.5-mm intracoronary shunt (Medtronic Clearview®, Minneapolis, MN, USA), at a point midway between the apex and the base of the heart (Fig. 1). An end-to-side anastomosis from the LIMA to the LADV was accomplished, by use of non-absorbable monofilament sutures (Prolene® 8–0). Immediately before completion of the anastomosis, the intracoronary shunt was removed. The LADV was ligated proximally to the anastomosis (~2 cm) and the LAD was also ligated at its midpoint, with silk sutures (Silkam® 2–0; B Braun Medical, Oeiras, Portugal). The temporary atraumatic clamp (Geister T03, Tuttlingen, Germany) used at the LIMA was then released, and observation of blood flow from the LIMA to the LADV confirmed the integrity of the anastomosis.

Exactly as for the control group, an intravenous injection of 5000 IU heparin was administered prior to LAD occlusion. This was followed by daily intravenous administration of acetylsalicylic acid until the fifth day after surgery. Chest closure and placement of chest tubes was performed as for the control group.

The surviving animals were killed on the fifth day. For comparison of cardiac performance and the affected myocardial area between the two groups, the same experimental conditions were used for both groups, and quantification of cardiac biomarkers, ECGs, echocardiography and detailed histological studies were performed blindly by independent investigators. A brief description of the diagnostic methods is stated here; more details are found in another report [6].

Cardiac biomarkers included troponin I, myoglobin, total creatine kinase, isoenzyme MB of creatine kinase (activity and mass assays) and lactate dehydrogenase. Serial blood samples were collected via a central venous catheter prior to surgery, every 2 h during the first 10 h after surgery and then every 24 h until the pigs were killed. Results are presented as the area under the curve (AUC) and peak values of each biomarker.

Electrocardiograms were performed prior to surgery and then 1 h and 4 days after surgery, whereas echocardiograms were done before surgery and 4 days later. Pigs were always under general anaesthesia during these examinations. For ECGs, precordial leads were included in order to determine the ventricular wall segment affected more precisely. For comparison of results, the sum of absolute ST segment deviation (elevation or depression) was calculated for all leads that measured 60 ms after the J

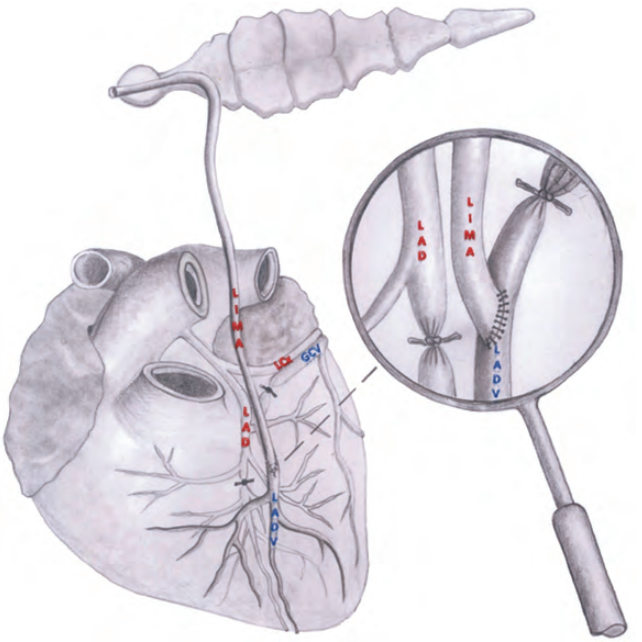

Figure 1: Schematic illustration of cardiac vessels, occlusion sites and arteriovenous anastomosis. GCV: great cardiac vein; LAD: left anterior descending coronary artery; LADV: left anterior descending vein; LCx: left circumflex artery; LIMA: left internal mammary artery.

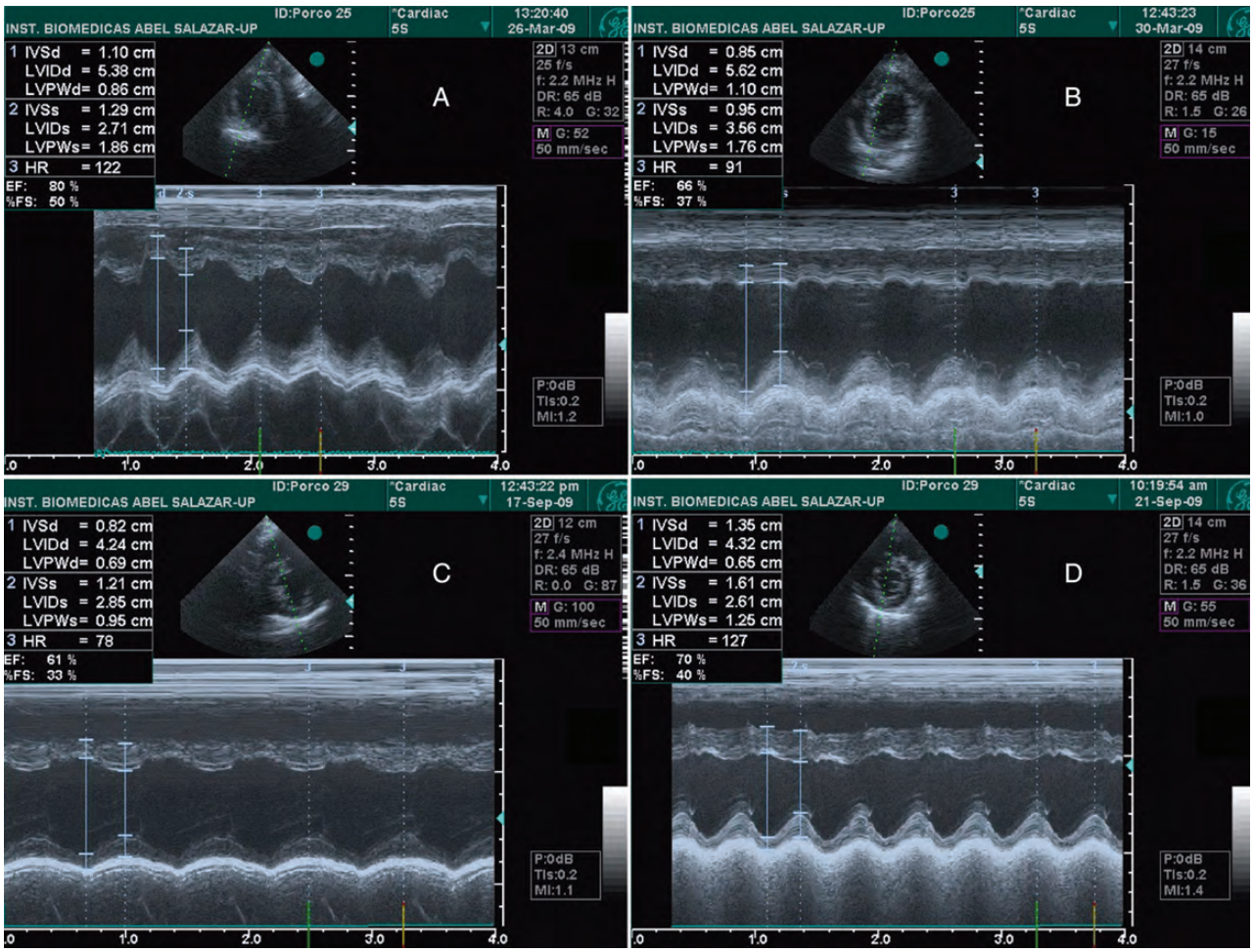

Figure 2: M-mode echocardiography in one pig from the control group, at baseline (**A**) and on the fourth day (**B**), and in one pig from the experimental group, at baseline (**C**) and on the fourth day (**D**). EF: ejection fraction; HR: heart rate; IVSd: thickness of interventricular septum at end diastole; IVSs: thickness of interventricular septum at end systole; LVIDd: left ventricular internal diameter at end diastole; LVIDs: left ventricular internal diameter at end systole; LVPWd: left ventricular posterior wall at end diastole; LVPWs: left ventricular posterior wall at end systole; %FS, percentage of fractional shortening.

point relative to the TP segment. With echocardiography, the ventricular wall contraction was visually evaluated, and measurements of the left ventricular lumen and wall thicknesses allowed calculation of the ejection fraction, for ascertainment of cardiac performance. Full design and data collection for both ECGs (method GUSTO-I) and echocardiography are described elsewhere [6, 7].

Histological studies were performed after the pigs were killed on the fifth day. Hearts were collected and fixed in 10% formaldehyde. For confirmation of complete arterial occlusion, the LAD was cannulated and, through injection of saline solution, visual inspection for leaks at the ligature site and absence of filling of distal arterial branches was performed. Likewise, the LIMA was cannulated for injection of saline solution to evaluate patency of the arteriovenous grafts and filling of the distal venous tributaries. The hearts were then sectioned in transverse slices (1 cm wide) from the apex to the heart base. From each of these slices, the full basal surface (including septum and both ventricles) was divided into small blocks, which were processed, paraffinized and stained with haematoxylin and eosin and Masson's trichrome. These stainings allowed recognition of infarcted and healthy myocardial areas, which were measured using specific software (Image®, National Institutes of Health) to determine with precision the percentage of infarcted myocardial area in each pig. To enhance the macroscopic difference of the extent of infarcts in the two groups, and for photographic purposes only, three hearts were selected (two from control pigs and one of the experimental group) and stained with 2% 2,3,5-triphenyltetrazolium chloride. The apical surfaces of their transverse slices (where infarcts were visually identified) were incubated in 2,3,5-triphenyltetrazolium chloride at 37°C for 20 min. With this stain, necrotic myocardium appears pale and viable myocardium stains dark red [8].

Statistics

Statistical analysis was performed using the PASW package, version 18.00. All data are presented as means ± SEM. For all the variables included in this study, a Kolmogorov–Smirnov one-sample goodness-of-fit test was used to confirm normality. Student's *t* test for independent samples was used when comparing means.

RESULTS

Four animals from each group (control and experimental) died either during or shortly after surgery, owing to technical

Table 1. Echocardiographic results at baseline and on the fourth day in each group

Group	EF (%)		IVSs (mm)		LVIDs (mm)		LVPWs (mm)	
	0 h	96 h	0 h	96 h	0 h	96 h	0 h	96 h
Control (mean ± SEM; $n = 9$)	59.8 ± 2.6	47.2*** ± 2.4	12.2 ± 0.7	8.4** ± 0.7	29.1 ± 1.6	37.2*** ± 1.7	12.5 ± 0.7	14.2 ± 1.1
Experimental (mean ± SEM; $n = 9$)	56.0 ± 3.3	53.9 ± 3.4	10.3 ± 0.7	10.8 ± 1.2	31.5 ± 2.4	34.2 ± 2.8	12.0 ± 0.8	13.5 ± 0.6

EF: ejection fraction; IVSs: thickness of interventricular septum at end systole; LVIDs: left ventricular internal diameter at end systole; LVPWs: left ventricular posterior wall at end systole. $^{**}P < 0.01$, $^{***}P < 0.001$ vs 0 h.

problems or the MI itself; therefore, we present here the results from nine animals in each group.

Electrocardiography

Control group. One hour after coronary occlusion, all ECGs presented ST segment deflections, as well as variable changes in heart rate and polarity of the T wave. The average sum of ST segment shift was 7.8 ± 1.9 mm. The ST segment changes disappeared completely by the fourth day postsurgery in six pigs. All pigs presented positive T waves at baseline, which shifted 1 h after coronary occlusion in three animals. Four days later, five pigs presented a negative T wave.

The average heart rate was 85.2 ± 3.1 beats/min at baseline and 86.8 ± 8.9 beats/min 1 h after surgery. On the fourth day, it had increased to 115.1 ± 15.4 beats/min.

Experimental group. ST deflections were present in all pigs 1 h after surgery. The average sum of ST segment shift was 3.8 ± 1.1 mm. On the fourth day, these ST segment changes were totally resolved in five animals. The T waves were positive in all pigs at baseline. One hour after surgery and at the fourth day, all ECGs except one displayed negative T waves. Heart rate was unchanged from basal values to 1 h postsurgery (80.0 ± 3.3 and 79.1 ± 4.3 beats/min, respectively), but it increased until the fourth day (122.4 ± 8.5 beats/min).

Echocardiography

Control group. The echocardiography performed 4 days after surgery revealed a severe impairment in contractility of the interventricular septum (example in Fig. 2A and B). The ejection fraction decreased by 21% ($P < 0.001$), with a reduction of 31% ($P < 0.004$) in the thickness of the interventricular septum at end systole and evidence of enlargement (28%) of the left ventricular lumen ($P < 0.001$; Table 1). The thickness of the posterior wall did not show significant differences ($P = 0.207$; Table 1).

Experimental group. After surgery, the ejection fraction was similar to baseline (Table 1; example in Fig. 2C and D). Regarding the measurements of the left ventricular wall and lumen, there were also no changes, as can be seen in Table 1.

Figure 3: Transverse cardiac slices from one pig in the control group (**A**) and one pig in the experimental group (**B**), stained with triphenyltetrazolium chloride (×1.0 magnification). (A) From the total of seven cardiac slices, the five shown here presented lesions; the infarct was transmural in both ventricles and mainly located at the left part of the interventricular septum and anterior wall of both ventricles. (B) From a total of eight cardiac slices, only the three shown here were affected; the area of lesion was hardly recognized, but mainly located at the subendocardial part of the interventricular septum.

Histological studies

Control group. At postmortem examination, complete occlusion of the LAD at its mid-point was confirmed in all pigs. Histological results were fairly similar among the different animals. The total measured area of MI was 13.7 ± 1.0%. Within this area, necrotic tissue occupied 5.5 ± 1.0%, while the surrounding granulation tissue occupied 8.2 ± 0.5%. Infarcts were transmural in both ventricles, with the main area of lesion being located at the interventricular septum (Fig. 3A).

The total infarcted lesion in the left ventricle was more extensive than the one in the right ventricle (14.8 ± 1.2 vs. 10.8 ± 1.9%; $P = 0.048$). Granulation tissue was present in identical proportions in both ventricles (7.9 ± 0.8% in the left ventricle and 9.3 ± 1.7% in the right ventricle; $P = 0.47$); however, the left ventricle had a much wider necrotic area compared with the necrotic area in the right ventricle (6.8 ± 1.3 and 1.5 ± 0.5%, respectively; $P = 0.03$).

Experimental group. Postmortem examination confirmed that total occlusion of the LAD at its mid-point was achieved in all animals, as well as a patent arteriovenous anastomosis. The measured MI lesion in this group was 6.8 ± 1.2%. Within this area, necrotic tissue occupied 1.6 ± 0.5%, while the surrounding

Table 2. Average peak values and area under the curve of cardiac biomarkers in each group

Group	cTnI		Myoglobin		MMB	
	Peak (ng/ml)	AUC	Peak (ng/ml)	AUC	Peak (ng/ml)	AUC
Control (mean ± SEM; $n = 9$)	47 ± 7	2.989 ± 344	703 ± 95	10.441 ± 874	19 ± 5	537 ± 190
Experimental (mean ± SEM; $n = 9$)	46 ± 8	2.406 ± 194	586 ± 109	9.915 ± 1.788	18 ± 6	472 ± 114

cTnI: concentration of troponin I; MMB: mass assay of creatine kinase.

granulation tissue occupied 5.2 ± 0.7%. Infarcts were transmural in only three hearts. The other six hearts displayed subendocardial or scattered areas of lesion (Fig. 3B).

The left ventricle was more affected than the right ventricle (7.7 ± 0.9 vs. 3.9 ± 0.3%; $P = 0.0026$). The granulation tissue was present in identical proportions in both ventricles (5.6 ± 0.6% in the left ventricle and 3.9 ± 1.3% in the right ventricle; $P = 0.28$). In the left ventricle, the area of necrotic tissue was only 2.1 ± 0.7%, while the right ventricle did not present any necrotic areas.

Cardiac biochemical markers

In both groups, the concentrations of cardiac biomarkers increased rapidly within the first 10 h and then slowly decreased until the fifth day. Differences in the curve shape, peak values and AUC were observed between individuals within each group. The AUC and peak values of troponin I, myoglobin and mass assay of creatine kinase (MMB) are shown in Table 2.

DISCUSSION

Our optimized model

Retroperfusion through the coronary sinus or arterialization of selected cardiac veins has been performed in experimental animal models (and even in a few human patients), mainly during the 1970s. Despite the obsolete diagnostic methods used, several scientists have provided good evidence that, in the acute phase of MI, these techniques are able to perfuse the myocardium, maintain metabolism, limit infarct size and maintain left ventricular function [9–16]. After the 1970s, research on cardiac venous arterialization was much reduced and only scarce literature can be found, probably as a result of the success of the two newly developed techniques, namely angioplasty and surgical bypass [8, 17–22]. The most remarkable reports published after the 1970s concern the development of catheter devices to arterialize veins, thereby avoiding surgical invasive approaches [21, 22]. In one of these studies [21], the catheter was introduced from the proximal LAD to the LADV. However, these trials were not very successful, mainly due to variations in vascular anatomy and technical problems. In the second study [22], the LADV was arterialized directly from the left ventricle, but the lack of a valve resulted in backflow into the ventricle and low venous pressure.

Our research aimed to optimize selective cardiac venous arterialization and measure its benefit. Our strategy is quite different from those reported in previous studies, as follows:

(i) We used the pig as animal model, instead of dogs and sheep which were used in former investigations [16, 18]. Pigs are a more appropriate experimental model because their arterial and venous cardiac architecture resembles that of humans and they display a relative lack of natural collateral circulation [6, 10].

(ii) We have compared our results with a control group of animals subjected to LAD ligation only. Most previous studies, however, did not establish these comparisons and thus could not really evaluate the benefit of cardiac venous arterialization. Hochberg *et al.*, Møller *et al.* and Harig *et al.* were three of the few groups who performed these comparisons [16, 19, 20]. However, the LAD was occluded more proximally in these studies, which resulted in early death of all control animals, thus impeding the collection and comparison of cardiac data during the following days.

(iii) We have applied several more accurate diagnostic examinations to evaluate the benefits of cardiac venous arterialization. Thus, unlike previous studies, quantitative analysis of left ventricular function and precise evaluation of the reduction in infarct size was made possible [9–16].

(iv) Our team employed up-to-date anaesthetic agents and surgical equipment. Also, as recommended for anastomotic surgeries, heparin and antiplatelet therapy were administered to prevent clotting from interfering with blood flow through the arterialized cardiac veins.

(v) In the experimental group, the LIMA–LADV anastomosis was opened immediately after LAD ligation, so the area at risk was never exposed to ischaemia. The following two main reasons justified this procedure. (a) Despite the standardized timings of ischaemia, the individual LAD distribution creates variable amounts of necrotic tissue before venous arterialization is active. Necrotic tissue is irreversibly damaged, and will not be recovered even if within the area perfused by the arterialized LADV. It would be impossible to perceive whether necrosis was due to the induced ischaemia or to inefficiency of the arterialized LADV. (b) Also, the induced ischaemia would increase the number of deaths in the experimental group. Would they be caused by a wider LAD arborization, by an abnormally long exposure to ischaemia, by an extended surgical procedure and/or increased recovery periods, or simply by the limited revascularization capacity from the arterialized LADV? All these variables would overshadow the real benefit of venous arterialization. In our study, by not inducing ischaemia, quantification of the exact perfused/non-perfused myocardium by the arterialized LADV was made clear.

The information provided by our research is limited to the acute phase of MI, and the animals lacked any atherosclerotic disease; therefore, further investigations should focus on the patency of grafts in long-term studies and in atherosclerotic animal models for translation into the ischaemic disease in

humans. Chowdhry *et al*. have experienced poor results with the patency of arteriovenous grafts, although all four patients were free of angina 2 years later [2]. Three reasons might explain this failure of graft patency, as follows: (i) the saphenous vein was used as a conduit between the aorta and the middle cardiac vein, so two anastomoses and a longer circuit were used; (ii) in each patient, two additional arterial grafts were performed at major coronary arteries, which could have led to a higher capillary pressure; and (iii) collateral circulation might have developed during those 2 years.

Analysis of results

In our experimental group, three deaths were caused most probably by anatomical variations (thin LIMA, bifurcated LADV and overdeveloped LAD) and one was due to technical problems (after extubation, the position of the epiglottis was changed during transportation and delivery to the animal's quarters, leading to respiratory arrest and death). Regarding the control group, three deaths were due to the induced MI, while the other one seemed to be a result of technical problems (the pig was not stable enough to be moved to the recovery room).

In the experimental group, there was still a clear ST segment deflection 1 h after surgery, indicating the presence of MI. Nevertheless, these changes were less pronounced than in the control group, as revealed by the sum of absolute ST segment shift (50% lower in the experimental group; $P = 0.038$), one of the strongest ECG predictors of mortality [7]. On the fourth day, complete resolution of these ST deflections was recognized in about half of the pigs in each group. Also, in both groups the ECGs presented T wave shifts and tachycardia. Although not as specific as ST segment deflections, these two events are also common in MI [23].

After surgery, echocardiography in the experimental group showed that left ventricular wall thicknesses and contractility remained unchanged. The control group, on the contrary, suffered a clear decline in ejection fraction, with thinning of the interventricular septum and enlargement of the left ventricular lumen. In the control group, the tendency for posterior wall thickening seemed to occur in order to compensate for the dysfunction associated with the interventricular septum.

Peak values and AUCs of all cardiac biomarkers analysed did not differ between the two groups ($P > 0.2$). There may be two reasons for this, as follows: (i) several studies have demonstrated that reperfusion to ischaemic tissues may exacerbate or accelerate injury, although the mechanisms are still not fully understood [24]; and (ii) we hypothesize that the impaired venous drainage (LADV was ligated) might have been another possible cause [23]. A study by Fredericks *et al*. suggests that troponin I in pigs is a suitable biomarker for myocardial damage, owing to its cardiac specificity [25]. In fact, in their retroperfused group, Harig *et al*. reported a troponin I curve that reached its peak at 4 h and then declined to basal values. They also documented a much lower troponin I concentration in their retroperfused group compared with all other groups at 1 h after surgery [20]. We did not observe any differences between our two groups during the first hour, and peak values were reached at the same times. We believe this phenomenon requires further investigation. In our study, because troponin I and MMB are considered to be the most reliable biomarkers for their cardiac specificity and myoglobin can detect MI as early as the first 12 h, only the results for these biomarkers are presented in Table 2.

The percentage of histological lesion in the experimental group was 50% lower than in the control group (with $P < 0.001$), with a large difference (70%) in the amount of necrotic tissue (5.5 ± 1.0 vs $1.6 \pm 0.5\%$; $P < 0.001$). There was also nearly 40% less granulation tissue in the experimental group (8.2 ± 0.5 vs $5.2 \pm 0.7\%$; $P = 0.003$). In both groups, the lesion was mainly located at the interventricular septum.

In conclusion, all our cardiac data evidenced a severe MI in the control group, with high concentrations of cardiac biomarkers, changes in electrical activity reflecting a high value in the sum of ST segment deviations and a strong impairment in contractility of the left ventricle, especially from the interventricular septum. A high percentage of infarcted myocardial lesion (~14%) was identified in those animals. In the experimental group also, MI was identified by the rise of cardiac biomarkers, changes in ECGs and by histological studies, but no dysfunction was revealed by echocardiography on the fourth day. Moreover, the changes detected in ECGs were of lesser amplitude than those of the control group and, most importantly, the percentage of histological lesion was much lower than in the control group. Curiously, cardiac biomarkers remained as high as in the control group and did not correlate with the results from the other diagnostic tests. This phenomenon would require further investigation.

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Conflict of interest: none declared.

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ORIGINAL ARTICLE

eComment. Cardiac venous arterialization in acute myocardial infarction

Authors: ***Sevket Balta, Murat Unlu, Mustafa Cakar and Sait Demirkol***
Gulhane Medical Faculty, Department of Cardiology, Ankara, Turkey
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We read the article by Munz *et al.* with interest [1]. They aimed to investigate the benefits of cardiac venous arterialization in reducing acute myocardial infarct size and its effects on cardiac performance. This study revealed that selective cardiac venous arterialization can nourish the myocardium and is able to reduce the infarct size by more than 50%, while protecting cardiac performance. The study is successfully planned and the results are presented well — thanks to the authors for their contribution.

In the absence of collateral circulation, coronary occlusion causes myocyte necrosis, the extent of which correlates directly with the speed and duration of the occlusion. Early reperfusion of an ischaemia related artery (IRA) would decrease myocardial necrosis, improve left ventricular (LV) function, and reduce mortality rates. Opening an occluded IRA, whether early or late, produces survival rates disproportionate to the amount of myocardium salvaged.

A current trial clearly showed that in patients diagnosed with acute coronary syndrome, an early invasive approach is superior to a conservative approach [3]. Early reintervention may limit the extent of myocardial cellular damage compared with conservative medical strategy in patients with myocardial ischaemia due to early graft failure as well as in patients with acute myocardial infarction [4]. Myocardial reperfusion has been shown to improve both short- and long-term survival in patients who have experienced an AMI. The open artery hypothesis suggests that survival after AMI depends on improved LV remodeling and healing, electrical stability, and myocardial perfusion rather than on the reduction of the infarct size (i.e., myocardial salvage) [5]. Studies showed that late patency of an IRA, as opposed to persistent occlusion, was independently associated with better 1-year survival. In a long-term follow-up study of 505 patients who underwent percutaneous transluminal coronary angioplasty for post-MI ischaemia, 22 patients with an open IRA had a lower 5-year mortality rate than patients with a closed IRA. This held true even for patients with LVEFs <0.50.

Conflict of interest: none declared

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