

## Knowing where we are, knowing where we are going

### To the Director

The world population over 60 years of age is increasing: 8% and 11% in 1950 and 2009 respectively, and 22% is expected by 2050; (1) this tendency has also been observed in the CONAREC III (60.9 years), ESMUCICA (62 years) and CONAREC XVI (63 years) registries. (2) A subanalysis of the CONAREC XVI Registry (3) showed that there are also more obese patients, with increased post-surgical morbimortality, and a study carried out by our team showed that, over the past 11 years, our population has also aged, and has increased demand for emergency surgery. (4) The CONAREC XVI population has more hypertension, dyslipidemia, diabetes, chronic kidney failure, and more admittances due to heart failure and requirement for emergency surgery. However, mortality in artery bypass surgery has decreased (CONAREC III 11.8%, ESMUCICA 5.1%, CONAREC XVI 4.3%). As mentioned by Lowenstein Haber et al in their study, (2) this could be due to improvement in surgical procedures and postoperative care. Still, we are far from the international average. There are multiple causes, but a fact could be the tip of the iceberg of our reality: the use of intra-aortic balloon pump counterpulsation (IABP) during postoperative stage was 3.5% versus 23% of low minute volume syndrome. This makes the authors suppose that it is due to lack of availability, which leads me to ask: what other elements do many surgery centers in Argentina lack for the care of these patients, who are increasingly older, increasingly ill?

As Lowenstein et al stated regarding surgery without ECC, given the heterogeneous population and the type of study, it is difficult to draw conclusions. In the ROOBY Trial, (5) surgery without ECC had a higher combined endpoint at one year (9.9% vs. 7.4%;  $p = 0.04$ ), and in the work by Hu et al, (6) surgery without ECC was associated with more major vascular events (43.8% vs. 41.2%;  $p = 0.002$ ) and with the need for artery bypass surgery ( $p = 0.03$ ) at 4.5 years. Therefore, I think patients who can benefit from one technique or the other should be picked out.

Regarding valve surgery and combined surgery, the conclusions already discussed do not differ much from those for these procedures. The lower rate of mortality and the increased use of mitral valve repair surgery in the ESMUCICA may be due to differences in the availability of means and in the number of patients from the centers who were included in the ESMUCICA. Registries like the CONAREC XVI are very valuable, but a permanent registry of centers that perform cardiac surgery would be essential to take measures that bring our findings close to those of the First World.

Blas Mancini, M.D.

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### Authors' reply

We thank Dr. Blas Mancini's interest and comments, which we consider appropriate.

It is a fact that the world population is ageing, which results in increased comorbidity in patients, and in the fact that pathology is more complex and with increased perioperative risk.

We are aware of the limitations of registries, and in our case we are just providing information about centers with cardiac surgery and residence in cardiology. We believe it is valid to understand that if there is little availability of balloon counterpulsation in centers with medical training, conditions in which surgeries are carried out in smaller facilities with no residence must be even more complex, possibly with different surgical outcomes.

The surgery registry of CONAREC XVI allows us to compare with other international registries, and shows us that, while we have improved over the past ten years, we are still far from the international standard.

As Dr. Blas Mancini well states, different substudies are under development, which will let us know in detail the surgical outcomes in Argentina. The first one is an exhaustive comparison between surgeries with and without ECC, (1) in which, despite off-pump surgery would be associated with a lower rate of mortality and major complications, it will be a task of further analysis to establish who would benefit from each type of procedure.

Another work in progress is the analysis of independent predictors of mortality according to the type of surgery. (2) This study is the first step of a project that has already started: the development of our own preoperative risk score for cardiovascular surgery.

The CONAREC XVI cardiac surgery registry is the merit of a large group of residents, and it is the aim of the Argentine Council of Residents in Cardiology to continue and reveal, through registries, the reality of our country. That is why the National Registry of Coronary Care Unit, CONAREC XVII, is currently being developed.

We believe that the spirit of union and teamwork, the cornerstone of CONAREC, is shown with the goals posed by our society.

**Diego Lowenstein Haber, M.D.,  
Fernando Guardiani, M.D., Pablo Pieroni, M.D.**  
By the authors

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## Changes in the Lipid Profile of Patients with Acute Coronary Syndrome within the First Days of Hospitalization

### To the Director

An old challenge in clinical research is to determine, in the context of acute coronary syndrome (ACS), humoral variables that can predict prognosis to establish behaviors that advance, postpone or intensify therapies. Lately, variability in post-ACS lipid profile has become the focus of attention, because old (1) and new (2) studies show controversies about the following: a) the interval to obtain a representative sample of the historical baseline value, b) the percentage of the change in time, c) the appropriate method for measurement, and d) the causes influencing variability.

Pitt et al (2) based their observations on the LUNAR study, which was originally designed to compare intervention with two lipid-lowering drugs, and report a slight reduction of the values of the lipid profile on the first and second days, and an increase on the fourth day.

Their conclusions contradict previous studies reporting significant and long-lasting reductions in TC and LDL-C, and increased TG, suggesting -though unclearly- that its evaluation could be extended up to 96 hours after onset of symptoms.

Siniawski et al (3) analyze this variability in detail:

1. They perform and compare the variables with local population.
2. The goal is to analyze the lipid variability by direct measurement.
3. A1-Apo levels are included, so the quality of HDL-C can be inferred for the effective one.

4. They analyze the initial lipid profile within the 24 hours of hospitalization, and present a short interval from the onset of symptoms to the collection of the first sample (7.7 h), which allows to observe an early reduction in a slot not considered in the LUNAR study.

5. They set out expectation of clinical applicability to characterize dyslipidemia and to determine therapeutic strategies.

6. They report that 50% of their ill population had greatly reduced baseline values of HDL and A1 Apo, from what it is inferred and confirmed that the increase in both values is likely to be the target in primary prevention.

The drawbacks in the pioneering studies are the small number of patients, the lack of division by sex and age group, and the poor description of variables influencing the outcomes, such as those generated by implemented therapies. Heparin, beta-blockers and others impact on cytokines, on acute phase reactants, and on free fatty acids, which are elevated. Other affecting factors are stress and changes due to hospitalization -such as diet, posture, and hydration status-, which, on a small percentage, contribute to situations to be clarified in future studies.

The clinical research carried out by Siniawski et al meets the parameters that search for and clarify the problem, and its findings are applicable in the daily medical practice; it tries to identify, at an early stage and in a high-risk population, the type and degree of dyslipidemia to start appropriate therapies in hospital, which always improve adherence.

**Dr. Diego Manente, Dra. Noemí Lago<sup>MTSAC</sup>**

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### Authors' reply

We thank Dr. Manente and Dr. Lago for their opinions.

We agree that early assessment of lipid profile and analysis of variations within the first hours of ACS is important in order to determine the type of dyslipidemia before admission, and the choice of the most appropriate lipid-lowering therapy. Moreover, as Dr. Manente and Dr. Lago pointed out, early therapy improves long-term adherence.

The most important studies on statin intervention in the context of an ACS included patients at a late stage: the MIRACL at 63 hours, the PROVE IT-TIMI 22 at 7 days, and the A to Z at 3.7 days of the onset of symptoms. (1-3) Baseline values of LDL-C were 124, 106 and 111 mg/

dl, respectively. Baseline value of LDL-C in the MIRACL study (the shortest time between the event and the inclusion) was closer to the admission value of our study; in the placebo group, the LDL-C concentration increased 12% at 16 weeks, and reached 135 mg/dl, similar to the value found by our group. In our study, variations in plasma concentrations of LDL-C were early, suggesting that the LDL-C levels reported in the PROVE IT and A to Z trials probably did not represent the values prior to ACS. Therefore, it is difficult to estimate which was the real effect of statins on plasma cholesterol in these trials. We believe that lipid-lowering therapy should begin in the early hours of the ACS, as soon as the lipid profile on admittance is available. This therapeutic approach would provide several benefits: a more accurate knowledge of the response to the medication administered, a better adherence, and probably a greater clinical effect.

The observed reduction in apolipoprotein A-1 levels and, therefore, in the reverse cholesterol transport, raises the need to design studies to compare drugs that reduce the concentration of atherogenic particles, with strategies that act on both lipid mechanisms of atherogenesis in patients with ACS. (4, 5)

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#### Correlation between Metabolic Syndrome and its Components with Pulse Pressure in Persons without Apparent Disease

##### To the Director

The work by Paragano et al, Correlation between Metabolic Syndrome and its Components with Pulse Pressure in Persons without Apparent Disease, (1) offers us a very interesting perspective on two highly topical issues such as metabolic syndrome –with an increased incidence due to obesity epidemic and impaired quality of life, which affect most of the world's

population, especially from developing countries–, and the determination of vascular function parameters such as –in this case– pulse pressure.

As stated by the authors, in addition to the limiting parameters –systolic and diastolic blood pressure–, there are two very important but somewhat underestimated parameters in the clinical practice: mean arterial pressure and pulse pressure.

The first one reflects primarily peripheral resistances, whereas the second one is related to arterial wall stiffness; these can be so independent that with the same mean arterial pressure, a normal or an altered pulse pressure can occur. The paradigmatic example with normal mean pressure and altered pulse pressure is the elderly patient.

Development of diabetes may be preceded by several years of resistance to insulin, with high frequency inserted in what is known as metabolic syndrome.

From early stages, patients with metabolic syndrome may develop non-enzymatic glycation of proteins, microalbuminuria, renal hyperfiltration in the context of a major sympathetic activation, and therefore, also have a higher frequency of left ventricular hypertrophy and vascular changes, such as increased carotid intima-media thickness, atherosclerotic plaques, increased speed of the pulse wave, and impaired endothelial function. (2)

It could be said that, from the cardiovascular viewpoint, they are 'almost' diabetic patients years before diabetes is installed, and that explains a higher cardiovascular risk than in normal subjects.

While the exclusion criteria of this work, from the methodological viewpoint, prevents one of the most common components of metabolic syndrome (arterial hypertension) and it is unclear how many of those 1,155 young and healthy individuals had metabolic syndrome (they would be between 7% and 45%, according to Table 2, which is based on the combination of criteria), it demonstrates, from the statistical viewpoint, the sum of metabolic factors that contribute to the deterioration of arterial function and to increased pulse pressure in this young population.

Probably, the difference would not be much bigger, but if criteria were combined, certain potentiation might even be expected. Although in population-based studies this can represent a difference of 1 mm Hg, several epidemiological studies have shown that, in terms of cardiovascular risk, every millimeter counts, and one of the explanations could be the early alteration of vascular function, as demonstrated in this clinical observation.

Pedro Forcada, MD

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### Authors' reply

We thank Dr. Pedro Forcada's interest and helpful remarks about our work. The goal of the study was to analyze the influence of metabolic syndrome (MS) and its individual components on the arterial wall stiffness, assessed through pulse pressure (PP). Different diseases, including hypertension, are associated with decreased arterial compliance. (1) With the intent to rule out a possible conflicting effect on the results, we have decided to exclude individuals with current or previous cardiovascular disease, and for that reason hypertensive patients were not included. Thus, the resulting PP value is influenced only by the factor analyzed.

Components of MS include abdominal obesity (waist circumference  $\geq 102/88$  cm, men/women), hypertension (systolic/diastolic blood pressure  $\geq 130/85$  mm Hg), hyperglycemia (fasting glucose level  $\geq 100$  mg/dl), and dyslipidemia (triglycerides  $\geq 150$  mg/dl and/or HDL cholesterol  $\leq 40/50$  mg/dl, men/women, fasting). (2) Since diagnosis requires the presence of three or more of these factors, the prevalence in the study population reached 10.5%. At the statistical corrector's request, a table including data about the individuals with and without MS was added, from which the mentioned result arises. However, if we consider a waist circumference  $\geq 90$  cm for men and 80 cm for women, given the current recommendations for the population of Central and South America, (3) prevalence would be 19%.

Finally, increased PP determined by MS was significantly higher compared with its isolated components, a fact that would indicate certain potentiation. Nevertheless, hyperglycemia in itself causes a sharp increase of PP, even greater than the sum of three or more factors. Therefore, changes in arterial compliance may be related to the effect of this single factor.

We appreciate the opportunity this space has offered us for adding information about the published work.

**Antonio J. Paragano, MD<sup>MTSAC</sup>**

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### Blade Balloon Septostomy to Enlarge a Restrictive Atrial Septal Defect in Infants under 6 Months: Immediate and Medium-Term Outcomes

#### To the Director

For some complex congenital heart diseases, non-restrictive atrial septal defect is essential in order to maintain adequate oxygen saturation or cardiac output, as it is well described by Peirone et al, (1) the authors of the excellent paper. They describe in detail the technique and outcomes on six patients with complex heart diseases, who depended on an atrial septal defect of this kind to survive, and were resolved with cutting balloon septostomy.

In the immediate neonatal period, conventional balloon atrial septostomy is effective in 70% of the cases. (2) However, at later ages, the atrial septum thickens and hinders the conventional procedure; alternatives have been proposed in order to create another ASD close to the anterior one, such as radiofrequency transseptal puncture and subsequent balloon septostomy, and even the stent placement in the atrial septum, (3) which are procedures with excellent outcomes in most cases.

Our experience with cutting balloon has been poor, because when we considered using them, the balloons we had purchased were recalled by the factory because they were defective. Therefore, we successfully performed subsequent balloon septostomy in nine patients with characteristics similar to those presented by Peirone et al, with similar outcomes but with greater difficulty in the pathway, because of the need to use larger final diameter balloons and shorter duration of the ASD.

However, the procedure and the outcomes described by the authors of the paper show that excellent outcomes can be achieved with a simpler procedure, whose only difficulty is the availability of cutting balloons with adequate size. As Dr. Faella very well points out in his editorial, the pediatric market is not significant for the companies, so the provision of suitable material for these procedures is sometimes difficult.

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**José Gabay, M.D.**

**To the Director**

When, on the night of Friday 25 June, I learned about José's accident, my first thought was 'It can't be true!' It's a mistake.

None of us can accept the departure of José at such an early stage in his life, when the happiness of sharing everyday life with him was in the short memory of the recent hours or days.

Sadness, frustration, helplessness, and many more adjectives overtake us all; but my message today aims at recalling those moments which José fully enjoyed with his fellows and friends, who in many cases –like mine– were both.

José was always smiling when he came to the hospital to work; he loved the subspecialty and –as everybody knows– his accurate technical expertise was excellent. But if there was something that particularly set him apart was his knowledge of clinical medicine in general and of cardiology in particular.

It was very rewarding for us, his older colleagues, to share the daily tasks with him, and also for the younger ones, whom he always taught the specialty. Here is another virtue to point out: his gift for teaching in a practice in which mistakes are not admitted.

All the people from the Interventional Cardiology section loved José for his medical abilities, but even more for his human and sensitive condition and for the peace and security transmitted to professionals, and more importantly, to his patients. Once again, the daily work was a passion for José, and fortunately his patients always noticed and appreciated that.

In this regard, all his colleagues at the hospital, the administrative and the section staff, and every one without exception have suffered a lot from his absence.

His fellows from the Argentine Society of Cardiology, staff, authorities, project partners, and members who attended the SAC congresses and educational sessions learned about his enthusiasm for this Society.

As Vice President and future President of the CACI, he gave his support to all the activities organized by the Board, like courses and congresses, and he collaborated and participated with great professionalism and affection in every project he was required.

I would like to say a few words about José Gabay the human being, not the doctor. He deeply loved his wife and his family, made up of cousins and old aunts, who have told me about their pain of his absence.

He was a passionate for cars, an irony of fate.

He enjoyed tennis, meeting friends, travelling to different destinations with his wife and friends. He enjoyed good food and a glass of good wine. He was fond of all the advances in technology, and he always had the latest mobile phone, the latest devices.

José, to meet you was to love you and enjoy your company. It still hurts to remember you, but there will come a time when we can talk about anecdotes and

mention your name with regret but without this huge pain of today.

It is very hard to say goodbye to a great friend, so my words end here.

**Liliana Grinfeld, M.D.** <sup>MTSAC</sup>  
Former SAC President  
Former CACI President

I would like to thank Liliana Grinfeld for giving me the opportunity to share this space to say goodbye to our great friend, José Gabay. I have little to add to what Liliana has already mentioned about José's professional activity, whom I had the good fortune to meet in 1993, when he started working as resident of the Interventional Cardiology Unit at Hospital Italiano. Since then, we have been forging a friendship that grew stronger and stronger every day. Many were the times I shared with José and Marta, his wife, well beyond the professional and academic context, in the Argentine Society of Cardiology (SAC), in the Argentine College of Interventional Cardioangiologists (CACI), and in the Latin American Society of Interventional Cardiology (SOLACI). Liliana has already pointed out his excellent professional conditions as interventional cardiologist in the daily clinical work, and his brilliant performance in different areas of the academic societies in which he participated. Personally, because I have shared a lot of time with José and his wife outside the professional sphere, I can give a proper opinion about his extraordinary conditions as a human being. He was an exceptional friend. We spent many nice holidays together with our families; in recent years, we also went to the same club almost every weekend, with mutual friends like Sergio Varini and Liliana Grinfeld, among others. We enjoyed his company a lot, on Saturday and Sunday tennis matches, sharing a coffee or a meal, or on long walks, which we used to reflect upon different issues. The news of his fatal accident on June 25 has touched us all tremendously. It has filled us with distress and helplessness. No one can resign oneself to accept such plan of destiny. We all ask ourselves the same question: Why did such a young and good guy meet so absurd a death? And of course, we will not find any logical explanation. They are simply things in life, which we cannot handle. José left us unexpectedly at the age of 47, perhaps in the prime of his life, and no one will ever take his place. As the singer and composer Alberto Cortés says, "When a friend leaves, a gap remains, which cannot be filled by the arrival of another friend..." But he will always be present in our memories. The enormous pain and sadness that overwhelm us today will slowly give way to the unforgettable image of this great person whose name was José Gabay. Thanks for having given me the opportunity to be your friend.

**Dr. Antonio A. Pocióv** <sup>MTSAC</sup>  
Ex Presidente CACI