With Imaging Techniques, Less is More… and Even Better

"Scientists use imagination to coordinate facts, whereas artists treat facts as stimuli for imagination."

Arthur Koestler

INTRODUCTION

The physician´s task of diagnosing the patient's disease is inextricably linked to his awareness of the patient's attributions, expectations and desires about the disease and about his life; as well expressed by William Osler:

"It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has."

And since a disease is not in itself an ontological entelechy, I wondered that while *"a good physician cures the disease; an excellent physician cures the patient, the one suffering from the disease"*.

With the excellent images of the internal organs provided by radioisotope imaging techniques, computer tomography and magnetic resonance imaging, the dangerous assumption is that specialists who process the images can make a diagnosis, or that it can be revealed by new and more accurate data measured by laboratories. Furthermore, this theory is believed to work in asymptomatic subjects, anticipating clinical diagnosis and preventing signs and symptoms.

Therefore, the need for an experienced physician who specializes in patients rather than in techniques and who uses clinical reasoning should have already ceased to exist.

These assumptions have confused many physicians, leading them to neglect key clinical aspects of the interview, physical examination and clinical judgment, and, at times, to be diverted along unexpected pathways by incidental findings without pathological significance, which entail further tests and even risky unnecessary interventions.

Physicians need to use imagination to understand the disease and the patient, in the same way as scientists and artists do (do we have something of both?), because as Arthur Koestler says: *"Scientists use imagination to coordinate facts, whereas artists treat facts as stimuli for imagination."*

Both the new digitized imaging techniques and the development of electronic medical records introduce a third party in patient-physician communication: the computer and its attention-consuming screen. This other cost of technology is observed in the colorful drawing that a young female patient –a 7-year-old artist– dedicated to her pediatrician, showing the girl sitting on the examination table, with her older sister and mother seated nearby, all of them smiling and the doctor sitting, staring at the computer... with his back to the patient. (1) Her young pediatrician, described as humble, compassionate and with innate kindness, was shocked and wrote a caption for the drawing: *"The economic stimulus bill has directed $20 billion dollars to electronic health care technology, mostly dedicated to funding the electronic health record incentive. I wish to know how much this technology will really cost us."*

During a round in the coronary care unit, a patient comments that she recognized the medical resident who had treated her on walk-in request only after listening to her voice. To my disbelief, as the physician was not only pretty but also had patent Afro-Colombian features, she added that she had not seen her face because it was hidden by the computer screen.

Now that we are living with this new computerized registration of medical records, we should try to avoid paying selective attention to the computer; the kind of attention we used to pay our patients and that, by error or omission, we have relegated to a second place. As sad and horrible as it may sound, it is becoming a new reality.

IMAGING TESTS IN ASYMPTOMATIC PATIENTS FOLLOWING CORONARY REVASCULARIZATION

It is often the case that after a revascularization procedure, be it coronary surgery or angioplasty, the patient often reminds the physician that he has not yet indicated a myocardial perfusion stress test, or that the physician indicates this test as a routine, even though the patient is leading a normal life and is physically active, without any angina symptoms.

The three main reasons generally used to recommend this test are surveillance for restenosis after percutaneous coronary intervention or identification of graft patency after coronary artery bypass graft surgery, and assessment of complete revascularization. (2)

However, despite what most patients and many physicians believe, the latest Clinical Practice Guidelines do not recommend its use.

The Guideline published in 2011 by the American Society of Echocardiography, with the collaboration of eight scientific societies (ASE, AHA, ASNC, HFSA, HRS, SCCM, SCCT and SCMR), called *"Appropriate Use Criteria for Echocardiography by the ACCF"* (Ap-

propriate Use Criteria Task Force), (3) suggests that: *"Stress echocardiography in asymptomatic patients less than 2 years following PCI is inappropriate, but the appropriateness after 2 or more years is uncertain."* Similarly, *"stress echocardiography in asymptomatic patients less than 5 years following CABG is inappropriate, but the appropriateness after 5 or more years is uncertain."*

In turn, the *"Guideline for Percutaneous Coronary Intervention"*, presented in 2011 by the American College of Cardiology Foundation (ACCF), the American Heart Association (AHA) and the Society for Cardiovascular Angiography and Interventions (SCAI) (4) classifies it with "Class III No Benefit recommendation, and says that Routine periodic stress testing of asymptomatic patients after PCI without specific clinical indications should not be performed (Level of Evidence C)". It explains that performing *"routine testing of all patients following PCI will also lead to many false positive test results, particularly in the era of "drug-eluting stents" (DES). As restenosis rate declines from 30% to 10%, the frequency of false positive stress testing results increases from 37% to 77%."* (4)

To understand that a positive stress test following angioplasty in an asymptomatic patient is generally false, we will review a meta-analysis on functional testing values to detect restenosis following percutaneous transluminal coronary angioplasty. (5) The meta-analysis shows that conventional exercise treadmill test (ETT) with a sensitivity (ST) of 46% and a specificity (SP) of 77% has a likelihood ratio (LR) of only 2.0, barely doubling up the probability after the test. Exercise nuclear imaging (ENI) with increased ST (87%) and equal SP (78%) shows almost twice LR (3.96), and stress echocardiogram test (SET), with less ST (63%) but the best SP (87%), shows the best LR (4.85), increasing the probability almost five times after the test.

Knowing that prevalence of restenosis in bare metal stents is approximately 30%, a positive test result following ETT increases the true positives only to 46%, but 54% (more than half) will be false positive results. Imaging tests (ENI and SET) (nuclear stress and stress echocardiographic imaging) with increased LR only show 36% and 32% false positive results, respectively.*

SEARCHING FOR THE FORGOTTEN CLINICAL SIGN: ANGINA

However, chest pain can be classified even without medical intervention, by simply completing the Geoffrey Rose *"chest pain questionnaire"*, in the modified version of the World Health Organization (WHO) (8) (Figure 3).

However, when these same tests are performed to detect restenosis in patients with drug-eluting stents with a prevalence of about 10%, a positive test result following ETT shows the huge proportion (81%) of false positives (since the true positives increased from 10% to 19% only). Exercise nuclear imaging and SET show 67% and 65% of false positive results, respectively (Figure 1).

Therefore, we can conclude that if an imaging stress test following coronary angioplasty is indicated for asymptomatic patients, in 2 out of 3 and even in 3 out of 4 patients with positive result, restenosis will not be detected in coronary angiography.

But despite the many false positive results, it is also known that the presence of ischemia in a stress echocardiogram predicts adverse results, even after an angioplasty. (6) However, there is no evidence that repeating the revascularization based upon a positive test result will change the progression of the disease or the patients' outcomes.

A recent publication on the outcomes of a retrospective observational cohort that prospectively used data from 2105 consecutive asymptomatic patients after PCI (54%) or CABG (46%) referred to the Cleveland Clinic (Ohio) from 2000 to 2010, (7) with a mean follow-up of 5.7 ±3.0 years, provides interesting information (Figure 2).

* In Bayes' theorem, likelihood ratio (LR) is expressed as the ratio of sensitivity (ST) divided by the inverse of specificity(SP) (1 - specificity):

$$LR = \frac{ST}{1 - SP}$$

Therefore, LR is expressed as an "odds", odds being the ratio of a probability (%) divided by the inverse of the probability (%) (1 - probability):

$$Odds = \frac{p}{1 - p}$$

Therefore, in the application of Bayes´s theorem, probability before the test, for example 30% in the bare stents, must become:

$$Odds = \frac{0,3}{1 - 0,3} = 0,43$$

So finally posttest odds will be equal to pretest odds multiplied by LR.
Posttest odds = pretest odds × LR. In the example of bare-metal stents we know that the prevalence of 30% restenosis has become the pretest odds of 0.43, so using ETT we have: 0.43 × 2, 0 = 0.86, which is the posttest odds. Now we convert the posttest odds in probability or percentage:

$$p = \frac{odds}{1 + odds}$$

$$p = 0,86 / 1 + 0,86 = 0,46$$

We multiply by 100 = 46%, which is the probability of a positive test to be a true positive, therefore, the probability of false positive is the inverse, i.e. 54%.

Only 1 out of 3 of 13 % ischemic patients underwent subsequent revascularization, but in 17% of the revascularizations performed, only in 1 out of 4 the indication was due to an ischemic test in asymptomatic patients.

Although mortality was associated with ischemia with a RR of 2.0, it was not an independent predictor, since in the multivariate analysis the only predictors were clinical. Low-risk patients were < 65 years, had no diabetes and were non-smokers, and even high-risk patients did not benefit from revascularization.

The study concludes that high-risk patients may be identified among asymptomatic patients who undergo stress echocardiography, but they do not seem to have more favorable outcomes with repeated revascularization. Furthermore, few patients with positive test results undergo revascularization, and within those few patients, even fewer cases are due to positive test results in asymptomatic patients.

SEARCHING FOR THE FORGOTTEN CLINICAL SIGN: ANGINA

Since Heberden's classical clinical description, we have learned that what he called angina is strongly associated with physiologically significant coronary lesions. We also know that if the LR in a positive myocardial perfusion test is 5.70, the LR in "typical angina" is 200; which means that, as a diagnostic tool for coronary ischemia patient interview is considerably better than any stress imaging test.

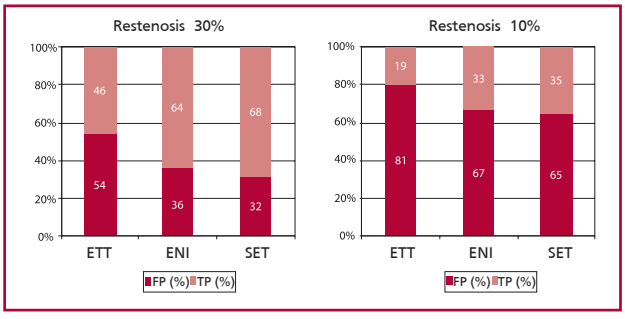


Fig. 1. Probability of false positives. ETT: Exercise treadmill test. ENI: Exercise nuclear imaging. FP: False positives.TP: True positives. SET: Stress echocardiogram test. With data from reference 5.

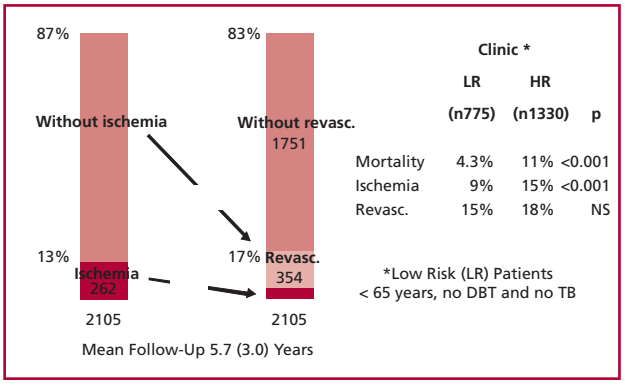


Fig. 2. Exercise echocardiography in asymptomatic patients following revascularization.

However, the experience of any cardiologist who treats patients in a coronary care unit is indeed discouraging, since many patients who are hospitalized as a result of acute coronary syndrome had already presented with undiagnosed typical angina symptoms, in some cases, because patients did not consider these transient symptoms a discomfort deserving medical consultation and, in many other cases, because angina had not been previously detected by the physician.

However, chest pain can be classified even without medical intervention, by simply completing the Geoffrey Rose *"chest pain questionnaire"*, in the modified version of the World Health Organization (WHO) (8) (Figure 3).

Two classifications of angina can also be applied. First, angina is classified into *"definite angina"* if the answer is Yes to four additional criteria: slows down or stops in response to chest pain (q 5), pain goes away when stopping (q 6), within 10 minutes (q 7), and pain location (q 2) including the sternum or the left anterior chest, and as *"possible angina"*, if only three out of the four additional criteria are met. (9)

In the 11-year follow-up of the Whitehall II (10) prospective cohort study on 10308 civil servants, participants completed five Rose angina questionnaires between 1985 and 1999. Surprisingly, at the time of the first angina report, 74% of participants diagnosed by the questionnaire had no diagnostic verification in their medical record and, even more alarming, 65% of those reporting angina again, still remained without medical diagnosis. The reader might think that diagnoses by the questionnaires and not by a doctor might be false diagnoses of angina; however, this was ruled out because, among participants with abnormal ECG, the absolute risk of non-fatal myocardial infarction was similar both in the group diagnosed by their doctor (16%) and in the undiagnosed group (15%). Thus, the questionnaire evidences the large proportion of the *submerged clinical iceberg* of angina.

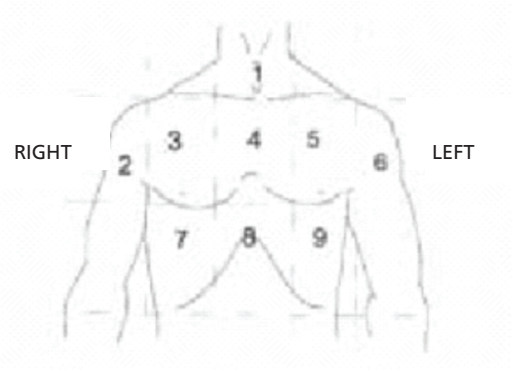
Typical angina is so important that prognosis of a significant lesion in at least one coronary vessel increases to 92% in a man aged 50-59 years. And despite having a negative imaging stress test, prognosis would only decrease to 67%, and still 2 out of 3 patients would have at least one significant lesion.

Therefore, in cases of typical angina, imaging stress tests do not add any information and may even lead to wrong results, since positive results can only confirm what we already know, and negative results cannot rule out significant coronary disease.

SEARCH OF ISCHEMIA IN ASYMPTOMATIC PATIENTS

While some physicians would accept that in the presence of a very high probability of coronary disease revealed by typical angina, imaging tests would not be necessary to decide medical procedure, most laymen and a great number of doctors assume that in asymp-

1) Do you ever have any pain or discomfort in your chest? *Yes *No
2) Where do you place this pain or discomfort?
(Mark the place(s) with X on the diagram.) (Numbers are only for the classifier.)



3) Do you have this discomfort when you walk normally on level ground? *Yes *No
4) Do you get it when you walk uphill or hurry? *Yes *No
5) When you have any pain or discomfort in your chest, what do you do? *Yes *No
- Stop
- Slow down
- Continue at the same pace

6) Does the pain or discomfort go away if you rest? *Yes *No
7) How soon does it go away?
- 10 minutes or less
- More than 10 minutes

(Modified by de Lampe FC, et al Am J Epidemol 2001,153:1173-82.)

Fig. 3. Chest pain questionnaire.

tomatic subjects, serial and systematic stress testing, with or without additional images, would help to identify coronary artery disease and prevent its risks.

They would be surprised to read the recommendations of the U.S. Preventive Services Task Force (USPSTF) on coronary artery disease screening with electrocardiography (ECG) at rest and during exercise, published a few months ago. (11)

It postulates a grade D recommendation of not performing ECG screening at rest or exercise in patients with a low risk of events (<10% at 10-year-risk of coronary artery disease events), which means that it discourages the use of that practice, since there is moderate to high certainty that the test has no net benefit or that the damage outweighs the benefits. This view also includes invasive and unnecessary overtreatment with the morbidity of labeling the subjects as sick due to false positives. It must be taken into consideration that with 2% prevalence, 96% of the test results are false positives.

It concludes: *"For asymptomatic adults at low risk for CHD events, a resting or exercise ECG is unlikely to provide additional information about CHD risk beyond that obtained with conventional CHD risk factors* (that is, Framingham risk factors) *and result in changes in risk stratification that would prompt interventions and ultimately reduce CHD-related events."*(11)

In asymptomatic adults at intermediate risk for coronary artery disease (10% to 20% of events at 10 years), or those at high risk of events (> 20% of events at 10 years) screening is not recommended, with grade "I" recommendation which states that the current level of evidence is insufficient to determine the balance of benefits and risks.

He concludes that: *"By omitting electrocardiographic findings, asymptomatic adults at increased risk of coronary artery disease are usually managed with a combination of diet and exercise modifications, lipid-lowering medications, aspirin, hypertension management and tobacco cessation. The net benefit of aspirin use and intensity of lipid-lowering therapy depends on the subject's baseline risk for coronary artery disease."*(11)

WHICH PATIENTS SHOULD BE SUBMITTED TO PROVOCATIVE TEST FOR ISCHEMIA WITH IMAGING TECHNIQUES?

It is clear that we often employ perfusion imaging not with diagnostic but with therapeutic purposes. For

example, when we try to identify the culprit vessel responsible for angina in a patient with multiple revascularizations, at least until we can safely measure fractional flow reserve (FFR) by means of multislice CT angiography. (12)

Although we know that in a patient diagnosed with high probability of coronary artery disease as a result of defined angina, complementary positive tests confirm what we already know, a negative result does not rule out the strong possibility of disease. And conversely, in low-risk asymptomatic patients positive tests are usually false and negative tests confirm our diagnosis. We are left with an intermediate range of coronary disease patients, in which we cannot arrive to a high probability diagnosis as they do not present all the clinical characteristics, or they manifest an uncharacteristic symptom, but similar to that manifested at the time of the heart attack. Moreover, if for any reason we have doubts when there is 40% to 60% probability of coronary artery disease, it is time for a provocative test for coronary ischemia.

If a man of 40-49 years of age presents with atypical angina, the probability of coronary artery disease is about 45%. If in this situation an ergometer test with myocardial perfusion is performed with a positive result (because the LR+ multiplies by 5.7), the probability after the test would then rise to 82% and lead to a high possibility of injury or significant coronary damage. If the result is negative (LR - multiplies by 0.19), the probability of coronary artery disease would decrease to 13% and pathologic coronary disease could be ruled out.

A SHORT HISTORY OF HOW WE DEVELOPED OUR DIAGNOSTIC ABILITY

Clinical medicine appears in 1760 when Giovanni Battista Morgagni is persuaded by his disciples to write in Latin (then the common language of scientific communications, as English is nowadays) the book of anatomopathological cases for disease identification, which he called *"De sedibus et causis Morborum. Per anatomen indagatis"* (The location and cause of the disease. Inquired by the anatomy), where in the thickness of the organs, visualized below the surfaces, diseases were localized and specified.

Forty years later, Xavier Bichat Paris, writes in *"Anatomie générale": "You may take notes for twenty-five years from morning to night at the bedside of the sick on the diseases of the heart, the lungs, the gastric viscera, and all will be to you only a confusion, which not being united in one point, will necessarily present a train of incoherent phenomena. Open a few bodies, this confusion will soon disappear, that observations alone would never have been able to dissipate"* As elegantly expressed by Michel Foucault, *"the living night is dissipated in the brightness of death"*. (13)

Bichat describes, for the first time what we call "tissues" in the *"Treatise on Membranes"* ("Traité des membranes", Paris, 1807), where he attempts to reduce organic volumes to large homogeneous surfaces that were called membranes. In *"Anatomie appliquée à la phsyiologie générale et à la medecine"* (Paris, 1801), Bichat recognizes in his discovery an event symmetrical to that of Lavoisier: *"Chemistry has its simple bodies which by various combinations form compound bodies ... Likewise, anatomy has its simple tissues, which by their combinations... form its organs."*(13)

Clinicians begin to look for signs that are no longer spontaneous, but the search of diseased organs and tissues. So Jean Nicolas Corvisart, Napoleon's personal physician, reactivates the old and forgotten discovery of percussion, that Auenbrugger had published as *Inventum Novum* in Vienna in 1760, the same year that Morgagni published *"De sedibus et causis Morborum"*. He translates it into French and thoroughly increases with personal cases the little book *"Nouvelle méthode pour reconnaître les maladies internes"* (Paris, 1808), where it is said: *"When a solid or liquid body occupies any part of the thoracic cavity, the side of the thorax, or that part so occupied, gives a duller sound"*

Such is the effervescence of the time with the burgeoning clinical medicine, that Corvisart dreams of completing Morgagni´s treatise with a book which, to paraphrase the title, he would call *"De sedibus et causis morborum per signa diagnostica investigatis et per anatomen confirmatis."* (The location and cause of diseases investigated by diagnostic signs and confirmed by anatomy). The initial circle closes with René Laennec's invention in 1819 of a device for listening to the thorax called stethoscope and introduced along with his book *"Traité de l'auscultation Mediate"* (Paris, 1819) (*"On Mediate auscultation"*). (14)

Physicians, armed with the patient's history, symptoms and signs, images and laboratory data, still continue to perform "retrospective prophecies" that allow them to infer from the observed effects, the preexisting cause or sufficient causes producing the effect, that we call cause of disease.

As Thomas Huxley claimed in 1888 the retrospective prophecy is the rationale of science *"historical or paleontological calls because they are retrospectively prophetic and strive for reconstruction of events in human imagination which have vanished and ceased to be."* And he summarizes *"if the method ... is legitimate for one science, it is legitimate for all"*. And it is doubtless the legitimate method that physicians use to make the diagnosis.

As it is impossible for our mind and also for the computer to make the diagnosis individually weighing the myriad of symptoms, signs, images and data, luckily our brain has the *"granulation"* ability, as modern fuzzy logic would say, the ability to gather attributes that although not equal have some similarity and degree of membership. Thus, it aggregates the findings into a set with blurred and uncertain boundaries that allow us to generate a list of plausible causes, and in turn make comparisons, instead of estimating the inaccurate probability of disease as a result of one particular finding. The heuristic rule of comparing two

diseases simultaneously is theoretically correct. If in each comparison what is most possible is always chosen, at the end, the winner will be the best diagnostic hypothesis.

CONCLUSIONS

To encourage *"things that doctors and patients should question"* about medical tests and procedures that may be unnecessary and in some situations could cause damage, more than 35 medical scientific societies, with the initiative proposal of ABIM Foundation (American Board of Internal Medicine), identified five commonly used tests or procedures in their field. They lit the spark to find out whether many frequently ordered tests or treatments are necessary, without being questioned or discussed.

Very recently (01/21/2013) 17 new lists were published of different medical societies on the *"five things that doctors and patients should question"*, on the website "Choosing Wisely". (15)

In the list of the American College of Cardiology the first two items say:

"Don´t perform stress cardiac imaging or advanced noninvasive imaging in the initial evaluation of patients without cardiac symptoms unless there are high-risk markers present.

"Low-risk asymptomatic patients account for 45% of unnecessary screenings. Tests should be performed if the following findings are present: diabetes in patients older than 40 years, peripheral arterial disease or an annual risk of cardiac events of more than 2%."

"Do not perform annual stress cardiac imaging or advanced noninvasive imaging as part of routine follow-up in asymptomatic patients.

"To perform stress cardiac imaging or advanced noninvasive imaging in a successive or scheduled pattern (e.g., every one to two years or on an anniversary of a cardiac procedure) in patients without symptoms rarely results in any significant change in patient management.

"This practice may in fact lead to unnecessary invasive procedures and excess radiation without any tested impact on patient outcome. An exception to this rule would be for patients with more than five years after coronary surgery."

In turn, the American Society of Echocardiography (ASE) writes:

"Avoid stress echocardiography in asymptomatic patients who meet a score of 'low risk' for coronary disease criteria.

"Stress echocardiography is primarily used in symptomatic patients to aid in the diagnosis of obstructive coronary disease.

"There is very little information on the use of stress echocardiography as a single standard test or added to conventional risk factors for the purposes of cardiovascular risk assessment in asymptomatic individuals."

Using the same criteria as the ASE, the American Society of Nuclear Cardiology in the first item says: *"Don't perform stress cardiac imaging or coronary angiography in patients without cardiac symptoms unless high-risk markers are present."*

And with the same criteria of the ACC states: *"Don´t perform radionuclide imaging as part of routine follow-up in asymptomatic patients."*

It adds in the second point: *"Do not perform cardiac imaging for patients who are at low risk." "Chest pain in patients at low risk of cardiac death or myocardial infarction (based on history, physical exam, electrocardiogram and cardiac biomarkers) do not merit stress radionuclide myocardial perfusion imaging or stress echocardiography as an initial test strategy if they have a normal electrocardiogram (without baseline ST abnormalities, left ventricular hypertrophy, pre-excitation, bundle branch block, intraventricular conduction delay, paced rhythm or on digoxin therapy) and are able to exercise."*

In turn, the Society of Cardiovascular Computed Tomography says: *"Don´t routinely order computed tomography coronary angiography for screening of asymptomatic individuals. Coronary computed tomography angiography findings of coronary artery disease stenosis severity rarely offer incremental discrimination over coronary artery calcium scoring in asymptomatic individuals."*

It also requests: *"Do not use computed tomography coronary angiography in high-risk patients in the emergency department presenting with acute chest pain. To date, randomized controlled trials evaluating use of coronary computed tomography angiography for individuals presenting acute chest pain in the emergency department, indicate that it has been lim*ited to low or low-intermediate risk individuals."

Finally, one should add that if we learn to *"choose wisely"* what the title says: *"with imaging techniques, less is more ... and even better."* will become true

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REFERENCES

1. KToll E. The cost of technology. JAMA 2012;307:2497-8. http://doi.org/k35
2. Eisenberg MJ. Routine periodic stress testing in asymptomatic patients following coronary revascularization. Arch Intern Med 2012;172:861-3. http://doi.org/k36
3. Douglas PS, Garcia MJ, Haines DE, et al. ASE / AHA / ASNC / HFSA / HRS / SCCM / SCCT / SCMR 2011 Appropriate Use Criteria for Echocardiography: a report of American College of Cardiology Foundation. Appropriate Use Criteria Task Force. J Am Coll Cardiol 2010. http://doi.org/cg3b8w
4. Levine GN, Bates ER, Blankenship JC, et al. ACCF / AHA / SCAI Guideline for Percutaneous Coronary Intervention: a report of American College of Cardiology Foundation / American Heart Association Task Force on Practice Guidelines and Society for Cardiovascular Angiography and Interventions. Circulation 2011;124:e574-e651. http://doi.org/d9n8jh
5. Garzon PP, Eisenberg MJ. Functional testing for the detection of

restenosis after percutaneous transluminal coronary angioplasty: a meta-analysis. Can J Cardiol 2001;17:41-8.
6. Cortigiani L, Sicari R, Bigi R, et al. Usefulness of stress echocardiograthy for risk stratification of patients after percutaneous coronary intervention. Am Cardiol 2008;102:1170-4. http://doi.org/cmpfww
7. Harb SC, Cook T, Jaber WA, Marwick TH. Exercise testing in asymptomatic patients after revascularization. Arch Intern Med 2012;172:854-61. http://doi.org/k37
8. Lampe FC, Whincup PH, Shaper AG, Wannamethee SG, Walker M, Ebrahim S. Variability of angina symptoms and the risk of major ischemic heart disease events. Am J Epidemiol 2001;153:1173-82. http://doi.org/bs84q6
9. Doval HC. En búsqueda del síntoma de enfermedad coronaria olvidado. Buscando la parte sumergida del iceberg clínico. Rev Argent Cardiol 2007;75:155-8.
10. Hemingway H, Shipley M, Britton A, Page M, Macfarlane P, Marmot M. Prognosis of angina with and without a diagnosis: 11 year of follow up in the Whitehall II prospective cohort study. BMJ 2003;327:895-8.
11. Moyer VA on behalf of the U.S. Preventive Services Task Force (USPSTF). Screening for coronary heart disease with electrocardiography: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2012;157. http://doi.org/dn8v85
12. Min JK. Diagnostic accuracy of fractional flow reserve from anatomic CT angiography.JAMA 2012;308:1237-45.
13. Michel Foucault. El nacimiento de la clínica. Una arqueología de la mirada médica. Siglo XXI; 1977.
14. Doval HC. El examen físico ha muerto: ¿debemos abandonarlo en un museo junto a la rueca y el hacha de bronce? Rev Argent Cardiol 2006;74:257-62.
15. www.choosingwisely.org.