To Test or not to Test: The Challenging Dilemma during Implantable Cardioverter Defibrillator Implantation Procedures

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The implantable cardioverter defibrillator is a life-saving therapy for patients at risk of sustaining a fatal cardiac arrhythmia. It is implanted under the skin over the chest wall pectoral area and has one or more electrodes that are inserted transvenously into the patient’s heart. The device monitors each and every heart beat and according to an algorithm is capable of diagnosing and treating ventricular arrhythmias that might otherwise lead to cardiac arrest.

Over the past 15 years, numerous randomized large-scale studies repeatedly demonstrated the efficacy of ICD therapy in various patients groups [1-3]. These were usually patients who survived a cardiac arrest episode, patients with a significant impairment of their cardiac function, or patients with an inherited disease predisposing them to malignant arrhythmias. Currently, most patients who are implanted with an ICD did not sustain a malignant arrhythmia but are implanted for the primary prevention of such an event. This also means that in the majority of patients the device will never treat (shock) an arrhythmia. Technologically, over the years the devices have become more reliable and more effective (i.e., they can deliver more energy). At the end of an implantation procedure (surgery) it was routine practice to test the device. Testing meant inducing ventricular fibrillation and letting the device diagnose and treat it (under sedation and with appropriately set backup external defibrillators). Furthermore, to define a defibrillation threshold (to evaluate the minimal energy required for successful defibrillation) multiple inductions of VF and subsequent defibrillations were performed during each procedure. To date there is no published randomized clinical trial sufficiently powered to answer the “to test (for defibrillation threshold) or “not to test” dilemma, although there is an ongoing trial, the “Shockless Implant Evaluation” study (SIMPLE http://clinicaltrials.gov/ct2/show/NCT00800384).

Against this background, Codner et al. try to shed some light onto the practice of defibrillation testing, and their results appear in this issue of IMAJ [4]. They retrospectively analyzed 213 patients implanted with an ICD of whom 80 underwent defibrillation safety margin testing (e.g., instead of defining the exact minimal energy required for successful defibrillation, they tested for successful defibrillation at an energy level 10 joules below the device’s maximum, thus performing fewerVF inductions). During a follow-up period of 2 years, there was no difference in overall mortality or in successful defibrillations performed by the devices for ventricular arrhythmias. Although this study deals with a highly relevant daily medical dilemma, its small scale makes interpretation of the results somewhat difficult. First, we do not know why some of the patients were tested and some were not. Can testing in the selected (higher risk?) group influence the outcome to give a null result? Second, we do not know whether all 80 patients were tested successfully or whether some were discharged for follow-up without an “acceptable” defibrillation safety margin (failed defibrillation testing). Last and most important, since current ICDs are quite successful at defibrillations, most defibrillation tests are successful. The same holds true for most real-life defibrillations of spontaneous VFs. Thus, to prove an advantage for routine testing or to show an equivalence of the two options with these highly efficient devices will require thousands of patients. Therefore, although the investigators found no benefit for defibrillation testing, there is a significant chance of a Type II statistical error, that is, the error of excessive skepticism. Nevertheless, since this study has high quality follow-up data, combining it with others [5,6] in a meta-analysis might have the statistical power needed to answer the dilemma of defibrillation testing.

At present, the clinical practice with regard to defibrillation testing during ICD implantation varies considerably, and it is not yet mandated by international guidelines [7]. Due to advances in device and
lead technology, and the growing number of primary prevention ICD implants on the one hand and the possible (yet very small) risk of complications during defibrillation testing on the other, a large number of implant procedures are currently performed without defibrillation testing [8]. Furthermore, the controlled testing scenario during an implantation procedure does not resemble a real-life setting in which fatal arrhythmias might be induced by electrolyte imbalance, acute ischemia, or other abnormalities. Thus, even successful testing might fail to predict defibrillation during situations in which the interaction between the ICD and the myocardium can be completely different.

Despite the data published by Codner and co-authors [4] and many other retrospective trials that do not reveal any benefit in defibrillation testing, the question whether to perform defibrillation testing remains to be answered by large and long-term prospective trials. The ongoing SIMPLE trial is aimed at clarifying this issue. The trial, which has already completed its recruitment, investigates the hypothesis that ICD implantation without defibrillation testing is not inferior to implantation with testing, the composite endpoint being failed first appropriate clinical shock or arrhythmic death. It also examines the hypothesis that defibrillation testing increases the perioperative (30 days) complication rate of ICD implantation. Currently, data show inconsistent center-dependent defibrillation testing approaches, underscoring the need for international guidelines regarding ICD implant testing.

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**References**


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**Capsule**

**IL-17A produced by αβ T cells drives airway hyper-responsiveness in mice and enhances mouse and human airway smooth muscle contraction**

Emerging evidence suggests that the T helper 17 (Th17) subset of αβ T cells contributes to the development of allergic asthma. Kudo et al. found that mice lacking the αvβ8 integrin on dendritic cells did not generate Th17 cells in the lung and were protected from airway hyper-responsiveness in response to house dust mite and ovalbumin sensitization and challenge. Because loss of Th17 cells inhibited airway narrowing without any obvious effects on airway inflammation or epithelial morphology, we examined the direct effects of Th17 cytokines on mouse and human airway smooth muscle function. Interleukin-17A (IL-17A), but not IL-17F or IL-22, enhanced contractile force generation of airway smooth muscle through an IL-17 receptor A (IL-17RA)-IL-17RC, nuclear factor κ light chain enhancer of activated B cells (NF-κB)-ras homolog gene family, member A (RhoA)-Rho-associated coiled-coil containing protein kinase 2 (ROCK2) signaling cascade. Mice lacking integrin αvβ8 on dendritic cells showed impaired activation of this pathway after ovalbumin sensitization and challenge, and the diminished contraction of the tracheal rings in these mice was reversed by IL-17A. These data indicate that the IL-17A produced by Th17 cells contributes to allergen-induced airway hyper-responsiveness through direct effects on airway smooth muscle.

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“The most erroneous stories are those we think we know best – and therefore never scrutinize or question”

Stephen Jay Gould (1941-2002), American paleontologist, evolutionary biologist and historian of science and one of the most influential and widely read writers of popular science of his generation