On the Need for a Universal Prospective ECG Database

Running title: Laks; Universal prospective ECG database

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Wolf-Parkinson-White (WPW) is one of the few clinical diseases that is mainly diagnosed by the electrocardiogram. One of the ultimate goals of modern medicine is to find a method to prevent disease. One of the best examples is catheter ablation of the Accessory Tracts in patients with WPW that will prevent tachyarrhythmias and Sudden Cardiac Death (SCD) in more than 95% of the patients. In patients with WPW, catheter ablation is the treatment of choice in the highly symptomatic patient with severe arrhythmias. A major challenge today is to ascertain the benefits versus the risks of doing catheter ablation in the asymptomatic patient with WPW. In this issue of *Circulation*, Obeyesekere et al using meta-analysis studied the risk of arrhythmia and sudden death in patients with asymptomatic pre-excitation and summarized the breadth of published evidence regarding the risks and benefits of catheter ablation in the asymptomatic patient. This study is an important milestone in the history of WPW, since its first description 82 years ago and ablation of AV conduction using a catheter was first accomplished in the dog 36 years ago and the first official report of its use in humans 21 years ago. The major conclusion of this meticulous review is that the available evidence is insufficient to justify the use of catheter ablation in the asymptomatic patient. This conclusion underscores the need to establish a prospective clinical and electrocardiographic database to determine the natural history of WPW (as well as other ECG abnormalities) from birth to death. Our arguments in support of this proposal are summarized below.

The Characterization of the Asymptomatic Patient

The first issue posed by these investigations is the need to establish a clinically relevant definition of the “asymptomatic patient.” Many patients presenting with an ECG diagnosis of WPW are not aware of the fact that they have this diagnosis and were also not aware of the association of arrhythmias. However, most of these patients do indeed have symptoms of
arrhythmias when carefully questioned. In fact, the investigators of this study considered some of
the categorized asymptomatic Italian patients\textsuperscript{1} should have been placed in the symptomatic
category. This need to better place these patients into well defined categories is critical to the
conclusions drawn from this study. This illustrates the limitation of gathering data from multiple
retrospective studies with different definitions of the asymptomatic patient. A major
recommendation for future studies would be the establishment of an agreed upon questionnaire
by experts with more precise definitions of a symptomatic patient. This problem demarcates the
need for a well designed prospective study.

**The Selection of the Data for the Database:**

Another issue is the high number of WPW publications excluded from this study. The
investigators utilized many high quality statistical techniques to validate the exclusion of a
marked number of published studies. Although well validated, in the final report only 3\% (from
an n of 590 to 20) of the published studies were adequate to use. Although the investigators did a
superb job of documenting the reason for these exclusions, they admitted that the exclusion of
case reports could have changed the incidence of mortality and morbidity in the asymptomatic
population. The original database that had to be significantly decreased to a valid database
further emphasizes the need for the creation of a well designed prospective ECG Database to
gather adequate information.

**The Incidence of Death in Patients with WPW:**

The most important issue is the limited data available to ascertain the risk-benefit ratio of
catheter ablation. The major question in this study is: what is the incidence of sudden cardiac
death in individuals with WPW? The unfortunate answer is that we have limited knowledge
because most of the sudden death individuals, particularly the young, did not have ECGs taken;
specifically under the age of 40 year old, less than 20% of the ECGs are available (Michael Ackerman personal communication). The use of a screening database of ECGs only by the Italian investigators is probably the explanation for the different results as described in this quotation from the publication of Obeyesekere et al: “the risk of SCD was statistically significantly lower in the non-Italian compared to the Italian studies.” Having a complete ECG database of patients with and without WPW is critical to quantify the burden of sudden cardiac death in individuals with WPW. In the publication, Obeyesekere et al attempted to answer this difference by evoking sampling bias in the non-Italian studies, confusion in the definition of asymptomatic, and the possibility of an increase in familial WPW in the Italian studies. This major difference in SCD between an organized and not organized collection of ECGs re-emphasizes the need to create a ”cradle-to-grave” ECG database.

The Risk of Catheter Ablation Procedure in WPW Patients:
The last important issue is: What is the risk associated with catheter ablation in patients with WPW? This question is particularly important in asymptomatic patients that have a low incidence of SCD. The authors state that: “The risks associated with an ablation procedure are likely at least similar to the risk of SCD in asymptomatic individuals.” This conclusion is supported by reports of 3 large series5 6 7. The investigators further appropriately state that these risks may be higher because they would be underreported in the community. However, these reported complication rates have questionable validity today because they were published almost 2 decades ago. I am in concert with the Pappone8 study, the current complication rate for catheter ablation of WPW cases is very low and the success rate is very high. This is the major reason for the need of a well designed prospective ECG database and outcome studies.

The Need for a Well Designed ECG Database:
There are excellent publications on decision making for catheter ablation in the individual patient with WPW\textsuperscript{9,10}. However, from all of the available studies that could be evaluated and analyzed, the major conclusion from the current meta-analysis is that the data are inadequate to make the appropriate decision to justify doing catheter ablations on asymptomatic WPW patients. This study highlights the need for a well designed ECG database with the inclusion of Holter monitoring and clinical data of patients for catheter ablation but also to discover patients with WPW and other ECG diagnosable diseases. Certainly, the cost will be high and must be balanced against competing economic demands with the marketplace. Furthermore a study must be carefully designed and phased in. It is axiomatic in the physical sciences that a complete description of any deterministic phenomenon requires knowledge of the values of the relevant variables and their rates of change over time. So too in clinical practice, when rational therapeutic decisions depend jointly on one’s assessment of the current level of risk, its concurrent rate of change, and the ability to reduce that rate of change. Conventional risk stratification schemas nevertheless refer only to the first of this triad. The first phase of a future prospective study would start with a pilot study of doing ECG. We agree with the investigators that an effective clinical database must include the goals of obtaining 1) the sensitivity and specificity of the test probably consisting of the delta waves and the PR Internals, 2) the cost-effectiveness of alternative treatment approaches, 3) the mortality and morbidity of the underlying condition 4) and the prevalence of the disease in different population strata. Most of these important goals could be extracted from a well designed ECG database. The cost effectiveness is an important determinate to calculate in order to justify the initiation of an expensive study. Although the information regarding the prevalence of asymptomatic WPW in the general population is limited, the cost-effectiveness of its treatment can be estimated from what data are available. Orejarena and
colleagues reported age specific-prevalence rates per 10,000 as follows: 0–19 years –2.0; 20–39 years –5.5; 40–59 years –9.6; > 60 years –4.8. Using a logistic model to fit these data, we estimate the prevalence of WPW at birth to be 1 per 10,000.

Since there are currently approximately 4 million live births annually, this means there are 400 cases of neonatal WPW being born every year. If we assume the average life expectancy of these newborns is 75 years in the absence of WPW and that WPW carries a lifetime risk of 33% (equivalent to an annual incidence of 0.44%) for sudden death, this amounts to a loss of 25 life years per case (a total burden of 25x400 or 10,000 years). If we further assume an ECG to cost $22.96 it would cost $92 million to detect these 400 cases, and an additional $5.4 million to treat them via catheter ablation ($13,389 per case). Thus the total cost for screening and treatment would be under $100 million and the total benefit (prevention of sudden cardiac death) is a gain in 10,000 life years. The resultant cost-effectiveness ratio of $10,000 per life-year is well under the current (albeit controversial) threshold of $50,000 per life year.

Clearly, this back-of-the-envelope estimate is flawed. The prevalence of the disease in newborns is not known, nor is the life-time burden in terms of life-years or quality-adjusted life-years lost. Treatment is not 100% effective at preventing sudden cardiac death and is not without its own inherent risk. Sudden cardiac death can still occur as a consequence of the later development of atherosclerotic disease. Finally, Medicare reimbursements do not represent actual costs, and even if they did, the cost of diagnosis and treatment in neonates is not likely to be borne willingly by payers given the current economic environment (witness the “doctor fix” enacted annually by Congress, in part to maintain reimbursement for ECG interpretation). But if these details are not sufficiently known, this is all the more reason to begin obtaining that information—to answer this question and to serve as a model to answer a spectrum of other
questions of similar potential importance to patients, physicians, payers and society-at-large.

Of importance in reference to high costs, a major logic for clinical decision making is related to the degree of tragedy of the disease entity that is under consideration; SCD has a high degree of tragedy. Therefore, even though the incident of this disease is very low, a society is more willing to spend more money and time to prevent SCD. In our culture, we spend a great amount of money on home fire insurance even though the incident of fire is low because the degree of tragedy is high. A well designed ECG database is needed. 

As medicine has been rapidly moving into the era of the curing of disease, what we will need are also moving rapidly in a computer technical world with the high capability to collect huge interactive databases as exemplified by the domains of Google, Face Book and particularly Wikipedia that exemplifies the dynamic and rapid updating of databases. The ECG has been one of the most used diagnostic tests in medicine and it is already in the computer digital wave format. We have to begin by developing the natural history of the human electrical signal coming from the heart from birth to death so that we can get correlative clinical data to better decode this cardiac signal so that we can improve our decision making not only in cases of WPW but all other electrical signals. Therefore, we will be able to obtain information that is from a database and not just from a single case report. The ECG signal can be made available from every human being on the earth by the appropriate health care providers.

At the time of the early development of the Acute Cardiac Care Unit at Cedars of Lebanon Hospital, I asked my mentor Jeremy Swan, “What benefit will we obtain from its
use?” He stated “We will get together patients in one part of the hospital with cardiac diseases that produce sudden cardiac death so that we can all carefully study it”. The same answer applies to the creation of a universal ECG database: we can all study the natural history of WPW as well as other ECG diagnosable diseases that produce sudden cardiac death.

**In summary**

Unfortunately, we do not get ECGs on asymptomatic patients so that we do not know the cause and the real incident of sudden cardiac death in WPW. Consequently, I agree with the recent publication of Philip Greenland and do not recommend that routine ECGs be done in the asymptomatic patient at this time. Of significance, we need to create a large ECG database that has to be started as a well designed research study to investigate the construction, contents and costs to answer the multiple questions posed by Obeyesekere et al. This study would focus on the true incidence of WPW and other ECG diagnostic abnormalities that can cause cardiac sudden death. Of importance, the major counterargument to the creation of an ECG Database is the actual cost.

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**References:**


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