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VIRTUAL LAF CONFERENCE

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SUBJECT: *Computer-Assisted Management of Atrial Fibrillation*

Hans has allowed me to present a software package I have written to manage my AF. The result has been so good that I wanted to spread the info to this board, but first a little recap.

I have been a frequent poster on this board for several years but took a break in February 2008. The main reason was that my then 14 years old daughter came to live with me and I wanted to spend as much of my time with her as I possibly could. She lives in Wyoming and I live in Sweden as a result of the insurance companies' use of a term they call "preexisting conditions" which is an effective way to close out unwanted people from health insurance in the US. In Sweden everyone is included in a national health insurance program and I had no choice than to go back to Sweden after I lost my insurance. I had posted about a drug protocol that I was using with good result, to fight my AF. Sotalol, Metaprolol and Diclofenak. The protocol gave me almost a year free from AF: 2007-12-28 to 2008-12-23 and the late half was totally without any arrhythmic drugs. Life was good!

I have been taking these pills, as I have needed them when in AF and the Diclofenak in between, 20mg one to two days, when I have felt a pain in my chest. I used the blood pressure and pulse as an indicator if I needed another pill. I have always, after I was refused my 6th el-cardioversion, used this protocol and returned to sinus rhythm. More than 200 times. When I have had longer attacks I have visited the local health clinic to have an EKG taken. The critical indication has been the QT/QTc interval that should be not less than 500ms. Sotalol as a potassium blocker increase this time and if to long there is a risk for ventricular fibrillation which can be a deadly condition. Anyway, at such a visit I happened to convert to sinus when I was standing at the reception desk and fainted. My QT/QTc was OK, 460ms, but my HR and BP obviously were too low just when I got into sinus. When I got home I started to write this software package, which I call PHM-AF. *Personal Health Manager-Atrial Fibrillation*. I had not written any software code for many years and when I did, it was more for process control, so it was a bit tough in the beginning. I had some ideas what I needed, but as the project rolled on, I added more functions. It has been hard to get to a stop as new ideas pop up all the time.

In my first try ever to put out info on a webpage, you can see some screen shots from the package. I will add more pictures as I go ahead and write about the program.
http://hem.bredband.net/fibrillations/

Luckily I had started to write down start/stop time for each AF-event and the pills I took to get the attack to stop at the end of June-08. I entered the data into a database and wrote code to handle data entry. See **pic 1**.
Dosage stands for a table where all changes in drug dosage are entered. It is convenient to compare this list with statistical presentations of AF-events in order to see if changes have any positive impact.

Pic 2 is a very simple bar chart of Af-events during a certain period, but I have found it to be very useful. Each bar represents a certain number of hours with fibrillation at a certain day. From the chart you can see that I am mostly a

vagal afibber as the attacks usually starts at night and continue in the following day, e.g. as it is one bar. Some attacks are coming very close after another attack. That is the result of that I have stopped to take the beta-blocker I take during an attack too abruptly. The next to last attack was unusually long, 38 hours, and was the result of that I changed the beta-blocker from nebivolol to bisoprolol and took to little of the drug. My heart tried to convert to sinus as usual after some hours, but went back to AF. The conversion act is accompanied with a strong adrenalin release, which drives up the heart rate and the strength of the contractions and it takes many hours to get back to a situation favourable favourable to a transition to sinus again. This has happened some times for me, so I recognize the situation. From the chart you can also see how I soon after got into another AF-event as a result of the massive drug intake from the long lasting event. Again you need to take a little beta-blocker, 2.5mg, about 3 days after the attack not to get into another one.

Pic 3. The program export data and instructions to Excel to draw graphics and make calculations. You do not need to know anything about Excel to get this picture. Just click on a button named Excel. This is very convenient, as someone that knows about how to use Excel, can make his own calculations. The first chart shows the duration of my AF attacks from July 2009 to March 2010. As you can see the trendline has a very favourable curve downwards, which means that the attacks are getting shorter. The other chart shows how the intervals between AF attacks are getting longer. The program controls Excel to make a regression analyze, where 6 different functions are tested with different parameters to get the best fit of the regression curve. You can read more about regression here:
http://en.wikipedia.org/wiki/Regression_analysis

The function that gives the best R-square value is plotted and the curve is extrapolated to the right with 10% of the maximal x-value used.

Instead of writing dates on the x-axis, days numbered from the start of the period are used. The first time I could use the system to write out an optimized list on how to take the pills during an attack, was the 21st of November 2009 which represents day no 144 and you can see how the upper trendline starts to bend down about there.

Pic 4. A very simple function of the program is to show how much time that has passed since the last attack. I have found this function to be very useful in order to take measures depending where I am in the periodical cycle of attacks.

Pic 5. In my next posting here, I will go through the PiP-procedures I have developed. From generating a list, when and how much of the pills that should be taken, to a closed loop analyze, where I can see how my earlier decisions of drug levels affect the length and frequency of my AF-events.

In the last post I will give my view on why my protocol is working. Hopefully I will get a break from AF at the end of April.

Gunnar

At the beginning of my AF career I was very symptomatic and visited the ER every time to get a cardioversion. Once they tried with Sotalol given as an IV-drip. It did not work. Next they used an infusion pump to drive the IV. After that they simply gave me a Sotalol pill and it worked. I was thinking a lot about that and realized that the only difference was, that I had taken a pill of Metoprolol extended release when the fibrillation started. I had got the pills from an American physician that had realized what was coming my way. After that I always took Metoprolol before I went to the ER and sometimes I converted before I was el-cardioverted. When I needed my 6th cardioversion, I was refused that from a physician I had not met before. He told me, that it was not meaningful to get another one as I had got one 3 month earlier. It is possible, that the fact it was a Friday afternoon had something to do with his decision. Anyway I talked him into giving me a Sotalol pill and some hours later I was in sinus rhythm. Finally I asked my physician, if he could prescribe me Sotalol, so I did not have to go to the ER to get a pill and so he did. Of cause, I wondered why the combination of Metoprolol and Sotalol was so effective. After some studies on the Internet, I found out that Sotalol is a drug with “a reverse use dependent property”, which means that it gets more effective in blocking the potassium ion-channels for outgoing potassium as the heart rate goes down.
http://content.onlinejacc.org/cgi/content/abstract/36/4/1404

You can say that an additional beta-blocker amplifies the effect of Sotalol and especially so a heart selective, beta1-selective, drug as Metoprolol or even better Bisoprolol. I have also used Nebivolol, which I went to Denmark to get hold

of. The trick is, that you get more effect with less Sotalol if you add a beta1-selectiv blocker and also fewer side effects from the beta2 –blocking from Sotalol, which affects all smooth muscles, like your intestines and arteries. You can here talk about synergy effects,
http://en.wikipedia.org/wiki/Synergy

And it gets even better, but more of that later. When I had got my database going and could produce some statistics, the question come up: When should I take the pills and how much should I take, when I had an attack of AF? From that I put a pill in my mouth I know the time or there about, when the drug has max-effect and also the half-life. See for example for Sotalol:
http://books.google.se/books?id=BfdighlyGiwC&pg=PA692&lpg=PA692&dq=sotalol+bioavalability&source=bl&ots=Krc8zMt32c&sig=f0TfzADtxq43iby0oocfVFR3gXs&hl=sv&ei=449xSrSYKInz_AbT18HcCg&sa=X&oi=book_result&ct=result&resnum=3#v=onepage&q=&f=false

I made an approximation that the build up and elimination of the drug was linear and could be represented by straight lines trough these points. There would be a positive error after the max-time and a negative error after the half-life, but the data was anyway given as “about-values” and it would probably be better than just counting pills, so I wrote some code, should be a lot of code, to calculate the build up and elimination of the drugs. In September I had a working function and could process my data from previous attacks one by one and could find an indication how much I should take of both drugs to achieve sinus rhythm within a reasonable amount of time. Here comes s a tricky part to understand. What my calculations show is not a concentration of the drug in my blood. I am not primarily interested in that. I am interested in a reference point, which I will arrive to at about the same time, the change to sinus rhythm, for a given amount of drug I swallow. I call that unit for a “Level” and make the assumptions that it is proportional to the concentration or it might actually vary for different amount of the drug. I do not care. The reason is that I analyse how long it took me to achieve sinus rhythm for a given amount at my previous attacks and use the same calculation every time. For instance the “Level” will be different for another person with a different body volume, kidneys that works better or worse, bioavailability, etc. I do not have any charts to show the result from these calculations as I between Christmas and New Years wrote code that implemented a more accepted way to calculate the elimination of a drug by the kidneys:
http://www.boomer.org/c/p3/c05/c0506.html

This is a first order linear differential equation which that can be evaluated to: Cp=A*Exp(-kel*t) and the constants A and kel can be calculated from the known points: time to max concentration and half-life. The result is shown in **picture 6**, where I as input has used times and amounts from an AF-event in July before I had started to write any code. The exponential decay, compared to the linear, looks better for the eye, but in real life the linear representation is good enough given the uncertainty of the data. Note how the drugs vary in concentration. No wonder you need too take a lot to get the desired effect accompanied with side-effects. Each curve represents a pill and the top curve is the sum of the underlying concentrations. If you now draw a vertical line at the number of minutes, when the change to sinus occur you will get the “Level”. Remember that I took these pills from the knowledge of the half-life and also from how my heart rate and blood pressure changed. There have been several tense moments, when I have wondered: Do I dare too take another pill? If the fibrillation has not ended in about 24 hours I have visited the local health clinic and asked them to take an EKG, so I could see what the QT/QTc was, e.g. if I was in danger of “torsades de pointes”. If not so, I have taken a little more of the drugs. It has worked fine. After all, I have converted to sinus more than 200 times by using this method and the worst has been that I once fainted when the conversion took place. You do however need to be extremely disciplined and have lots of patience and to stop before it goes out of control. In Sweden we have saying something like: “Too much shames everything. Enough is just right.” To be more blunt: Too much drugs will convert your heart rhythm to the eternal rest.

In November I had got so far that the program could produce a printout on how and when to take the drugs. Built in is a limitation of 8 pills/drug or 24 hours. See **picture 7** how you select which drug to use, the desired “Level”, Loading dose and Min dose. To get less variation I have started to take a half a pill of Bisoprolol. I am not doing it for both drugs as I do want to sleep some hours during the night and the current set-up is good enough. The printout is shown in **picture 8**. In **picture 9** you can see how each pill build up a concentration in the body and then leaves the body through the kidneys.

Gunnar

Gunnar,

This is an absolutely fascinating approach to afib management. Will this program eventually be available for other afibbers to use?

Hans

Yes, in a not so distant future. I will have to write a manual first. I also think that FDA has to give its permission, if it should be sold in the US. My main objective and priority has been to move myself out of a bad situation. AF-attacks every week is not fun.

Hans, you will be the first to receive a copy together with my database.

Gunnar

Gunnar, Nice work. Do you need an event monitor 24X7 to use your program?

Researcher

No. I am fully aware when I go into AF. Usually it starts with some PACs, but in many cases it starts while I am sleeping and wake up in AF. Then I have to empty my bladder with unbelievable amounts of fluids for a couple of hours.

I wrote about the attacks I sometimes get after a major run of AF, due to I am not taking any beta-blocker in between. I am warned in advance by a rising systolic blood pressure with a slightly elevated heart rate. A typical reading could be 165/65 and HR=60. My "normal" values with hypertension medication and a daily dose of Sotalol 20mg times 3 is 135/60 and HR around 50.

Gunnar

"*The critical indication has been the QT/QTc interval that should be not less than 500ms. Sotalol as a potassium blocker increase this time and if to long there is a risk for ventricular fibrillation which can be a deadly condition. Anyway, at such a visit I happened to convert to sinus when I was standing at the reception desk and fainted. My QT/QTc was OK, 460ms, but my HR and BP obviously was too low just when I got into sinus.* "

I don't know anything about the QT/QTc interval, however the "not LESS than 500ms" and "...was OK, 460ms" do not seem to go together, or am I missing something?

George

Got it thanks. Have you shown or talked with your cardiologist about the program? If so, please share any feedback.

My thoughts on the program would be that it would be best to leave the details in the background because I am not sure how receptive 70 yrs old folks to the technical details of gathering and inputting data. An intuitive user interface is probably needed where questions are asked of the patient of what drugs are being taken etc. It would be great if the program resides on the cardiologist's server and accessible through the internet such that results are immediately accessible by both patient and doctor remotely. Just some ideas. I have a beta tester for you whenever you think you are ready to go live.

Researcher

Sorry. A misprint from me. Should be less than 500ms.

A little surprised that you did not know anything about QT/QTc.

Supplementing with potassium can have the same effect as using a potassium blocker: a too long QT interval with the same consequences.

When supplementing with potassium, you increase the concentration gradient over the cell membrane, which makes it harder for potassium ions to leave the cell, thus prolonging the refractory period of the myocyte's repolarization/depolarization cycle.

http://www.cvpharmacology.com/antiarrhy/potassium-blockers.htm

You could say that QT time is a macro indication for the whole heart of what goes on in a myocyte in phase 1,2,3 and perhaps 4.

QTc is a kind of mean value. See
http://en.wikipedia.org/wiki/QT_interval#Correction_For_Heart_Rate

Gunnar

I wrote earlier that when I had that part of the program, Pharmacodynamics, which can print out curves of the AF-events I had entered from my notes, I printed them all out and tried to figure out what the best combination of Sotalol and Bisoprolol would be. The lack of overview made that task difficult. So when I had the Generator part working I started to write code that would figure out at what level I had conversion to sinus and the elapsed time to get there. The result can be seen in picture 10. As the amounts of Sotalol and Bisoprolol are so different, the first chart with both drugs does not show Bisoprolol with a resolution that will tell you anything. The program therefore instructs Excel to draw separate charts, as can be seen in the lower part of the picture. As usual a regression analyse is done and the trend lines are extrapolated this time to the left. The encouraging thing is that the theory of “reverse use dependency” for Sotalol is validated in the diagrams: Conversion comes at lower “levels” of Sotalol if the “level” of Bisoprolol is raised. I also made a special study that shows that in fact there is a negative correlation.
http://en.wikipedia.org/wiki/Correlation_and_dependence

Between Sotalol and Bisoprolol. I got most of the points from the time before I had any program. During September, October, November, December, January and February I used Nebivolol instead, but I varied the dose very little. Why change a winning combination? Now I have selected level 100 for Sotalol and level 10 for Bisoprolol and I might try 90 for Sotalol next time. The chart to the upper right shows that the more you take of the drugs, the shorter the heart will fibrillate, but one need to consider, that the heart can get to a full stop, if too much drugs are used. I am satisfied with 10 to 15 hours of fibrillation each time, as long as I can see a positive development. A couple of hours after the attack starts, I cannot feel the beats any more and can walk fast or do a little jogging (which I do not do). Without the drugs I was rather symptomatic. Anything faster than a very slow walk would drive up the heart rate to over 180 and continue to over 200 and I would faint, if I did not take a break. Now, under the influence of the drugs my heart rates varies between 85 and 100 during AF and I feel fine. I can even take a nap. My circulation is actually improved, as I can sit by my desk hour after hour, which is not true when in sinus, where the heart rate will go well under 50 and my legs and fingers well get swollen due to the suppression of my heart rate from the Sotalol (3 * 20mg daily). Another difference is that once the fibrillations stop, I am back to normal within an hour and is not worn down as I used to be before I used this protocol.

In picture 3 the top chart shows that I had two rather long attacks 39 and 35 hours each. My longest attack so far was 42 hours, but I cannot show any data. In all cases I had taken to little of the beta-blocker and the heart tried to convert at a more normal time, but then continued the AF-attack. My interpretation is, that there is a big release of adrenalin in order to start up to normal heart rate and blood pressure and it takes considerable time to consume that release and get back to more favourable conditions, if the transition fails. In picture 11 you can see my drug intake from the last long event, which had a bad impact on my statistics for February. I switched back to Bisoprolol in February, as I was out of Nebivolol and I simply overestimated the strength of Bisoprolol. When the attack had not stopped within 24 hours, I went to the local health clinic and had an EKG taken. My QT/QTc was OK. The physician would not let me return home and wanted me to be transported to the ER at the regional hospital. While waiting for the transport, I popped 1 pill each of Sotalol and Bisoprolol at about 9.00 and later while waiting for an el-cardioversion I converted to sinus at 12. When I was laying there, everything felt so quit and I rolled over on my side to take a nap. It then hit me that I should check my pulse and it told me I was back in sinus. Time to take the bus home.

All Excel sheets I have shown you are made by the program. Data and instructions are transferred to Excel when the operator clicks a button named Excel. This is rather advantageous, because if you are not happy with what you see and you know a little about Excel, you can make your own calculations or change the data. I was curious about how that long episode of 35 hours impacted the chart in picture 3, so I simply changed 35 to a more normal 15 hours and I must say I like that result much better, as seen in picture 12.

The 344 hours of sinus between events no 31 and 32 has also a little story. I was so happy that I had broken the recurring periods of AF-attacks so I went out to a Thai restaurant to celebrate the occasion. I love Thai food. When I got home again, I felt a bit sleepy, with my full tummy and decided to take a short nap. Veteran afibbers have probably already figured out what happened: I woke up after half an hour in AF. You really need a lot of patience as an afibber.

Next time I will write some words about my protocol and give my view on why it works so well. I think it is a sensation that an afibber since 2002 can change the path of ever-increasing attacks to a stop for almost a full year and then, perhaps, repeat that story again.

Gunnar

I had a routine visit with him in December and told him in advance that he should reserve some time so I could show it to him and he could give his view.

I bought a new lap-top for the occasion and the whole meeting was a disaster from my point of view. I was setup as his first patient that morning and when I got here it was chaos. The receptionist had not come. I think she had hit a deer with her car on her way to the job. Nurses and physicians stood waiting in the door while a substitute made her best to get thing going with registration and payments. After he had done his examination of me we sat down by his desk and I started the demo. Then his phone rang. As I could here from the conversation, his son had got ill at school and the teacher wanted to know if they could send him home or if anyone should come and pick him up. After that conversation I realized that the demo was over. By then he was off his schedule and stressed by the fact that his son was ill. His only comment was that it would be hard to set the amount of Sotalol and beta-blocker to give the patient at an attack and that you need extensive clinical tests to draw any conclusions. Come on! That is what he is doing every day as the chief cardiologist for the cardiology department. When I asked him, if I should continue what I was doing he said yes. At that point his highest desire was to get me out through the door.

I have another more interesting lead. I have contacted a school-mate, a physician, who now is a professor at Europe's largest hospital. He said the program and protocol might be of some interested as a task for his doctors(?). I am not sure if he just was trying to be polite, but I will come back to him after Easter. He is however not a cardiologist but has specialized in something which is called “open health care”, which is what is going on at local public health clinics.

Gunnar

Gunnar

Just for info if you want to study further the atria have a shorter action potential than ventricular myocytes, the atria express a channel called the Ikur which is an ultra rapid component of the repolarization of the atrial myocytes, this channel is not expressed in the ventricles

Have a read here
http://www.ionchannels.org/showabstract.php?pmid=15477405

Note that at the moment the Ikur is only a potential target for a channel blocker.

The current begins early and reaches maximum potential not long after phase 1 of the typical action potential

I know this is in regard to long QT syndrome genetics but this study throws out interesting questions.
http://www.escardiocontent.org/periodicals/yeupc/article/S1547-5271(07)00793-X/abstract

Conclusion in text
Our data indicate that the Q147R mutation can form the molecular substrate simultaneously for different arrhythmogenic conditions. The mechanism may be heterogeneous distribution of Kv7.1 accessory subunits in the heart leading to Kv7.1 gain of function in the atria (for AF) and Kv7.1 loss of function in the ventricles (for QT prolongation).

This particular mutation although rare when expressed in ventricular myoctyes causes loss of function, K+ isn't released from the cell as quickly and widens the ventricular action potential, the same mutation if expressed in the atria causes a gain of function mutation allows K+ to be released too quickly and shortens the action potential in the atria. How mad is that? and we know what shortening the action potential does in the atria.

Toni

Hi Gunnar,

I never studied about QT/QTc as I almost never use my little ECG machine. For my purposes, my Polar monitor tells me what I need to know - how many PVC's/PAC's per hour. It also tells me if I'm in afib - but I don't need it for that! It is much less hassle than the ECG.

My routine never pushes the envelope here. I've used PIP flecainide about 10 times in 5.5 years and the last 8 times, it converted me in an hour or less, so no need vary the flec dosage.

As to getting someone to look at your software. Perhaps when you have the manual written, someone here on he board who has a connection or good relationship with a "name" EP like Natale, Jais or Haissaguerre could make an introduction & you could make the presentation via a phone call & emailed files.

George

If you look at picture 12 and 13 there should be no doubt that I have reduced my AF both the length of the attacks and the total burden. Also the time between the attacks has become longer even if it now seems to level out. With my method of calculating how the drugs affect me I have in fact calibrated my method from the fact that I take 3x20 mg a day. For that reason I am reluctant to take some pills even if I can see an attack coming. In order to prolong the period between attacks I am now in the process of extending the program to be able to launch a preemptive strike http://en.wikipedia.org/wiki/Preemptive_war or perhaps I should say a prophylactic action. The problem as described above is that if I take some pills as I feel it coming, where should I set the “level” if the attack starts and still utilize the experience I have gained from earlier attacks. What the software will do is to allow entry of pills taken before the attack, calculate their elimination and if an attack occurs include those prophylactic pills in the elimination calculations from that point when the real starts. In that way I can achieve the right “level” that I have found suitable from past experience. So there is a new function added to the PiP section See picture 5.

With picture 14 I want to illustrate how little data you have to enter. When the attack stops you click on File and just enter the time. A default date can be accepted. The program will the store away the amount and time for the pills you have taken up to the given time. You rarely change the input: Drug, level and amounts, once you have found something that works.

I have been thinking a lot about how it is possible that I as seasoned afibber can get the AF to stop for a year from having weekly attacks and perhaps again stop it or at leas reduce the AF-burden with about 50%. I will sum up my thought in what I call **Gunnar’s protocol**:

1
I take Sotalol 3 times 20 mg per day in order to prolong the refractory period of the myocytes. What is important here is the potassium blocking property of Sotalol. I would prefer Tikosyn as that drug does not have the non-selective beta-blocking properties of Sotalol, but Tikosyn is not available in Europe.
http://cvpharmacology.com/antiarrhy/potassium-blockers.htm

2
I take, really, a rather low dose of Sotalol, but when I got to a stop of my AF in 2008 I started to reduce the amount of Sotalol I took. It was amazing how long it took to get to zero. At the end I took half a pill, 20mg every other day for a month, before I could stop the drug. If I during that month did not take the half pill I would have PACs. I stopped from 1 pill a day via ½ a pill and then ½ a pill every other day. I do want to take a small amount, as I do not like the side-effects from Sotalol , but also I want to be able to leave room in the heart rate, to take a cardio-selective beta-blocker if I experience intense PACs, e.g. several in a row. My heart rate back in 2002 without any drugs, when it all started, was a little above 50. The resting heart rate has become a little higher, but still under 55 so there is not much room to play with, if I also want to take a beta-blocker.

3.
When an attack starts, I immediately take a loading dose of Sotalol and Bisoprolol and use the program to print out the list on how to take the pills to get the most optimal effect with the least amount of drugs. Do note, that without this list I most likely would have to take bigger amounts with more side effects.
During the fall and winter of 2009 I took Nebivolol instead of Bisoprolol as that drug is even more cardio-selective.
http://en.wikipedia.org/wiki/Bisoprolol
Note it says:" However Nebivolol is approximately 3.5 times more â1-selective." Nebivolol is however not available in Sweden. It is approved as a drug for hypertension, but the importer is not offering it any more as the demand was to little. One reason for this might be that it is considerably more expensive than Bisoprolol. Bisoprolol also works but it has the drawback that the time for max availability is 3.5 hours compared to 1 hour for Nebivolol. To take Nebivolol is like taking placebo. Afibbers with a low blood pressure should perhaps stay away from Nebivolol, as the NO component might get the BP too low. I did however notice in my statistics that I had to take more of Sotalol and Nebivolol to get the desired effect; stop of the attack, compare to the combination Sotalol-Bisoprol. I did not vary the dosage enough to be able to get any meaningful correlation as for Sotalol-Bisoprolol in picture 10. I more or less stuck to the same dosage, as I was happy just if the attack would stop and was afraid of taking too much drugs.

4.
There is a synergy effect of taking Sotalol together with a cardio-selective beta-blocker because of the "reverse rate dependency" of Sotalol.
http://content.onlinejacc.org/cgi/content/full/36/4/1404
So again you do not need so much Sotalol. My worries have been that at long-lasting attacks, I would take too much drugs. For that reason the program is limited to only write out drug-lists for the first 24 hours or a maximum of 8 pills of each drug. You can come up to 8 if you take half a pill to get a more even load of the drug, which I think makes a difference as the load otherwise can vary with up to 30% at the optimal administration of the pills. After 24 hours it is time to get professional help with an EKG or perhaps a cardioversion. The later has not happened since I started this protocol after my 5th cardioversion.

5
I have wondered a lot about, why am I not following the expected path with less and less time between the attacks. In other words: why is it that "AF begets AF" is not working? My theory is that with the combination of Sotalol and a cardio or beta1 selective beta-blocker the electrical remodeling of the atria is not taking place or at least is not taking place with the same speed. There is much written about electrical remodelling. The Cleveland-Clinic has a written a article that is not too technical. See: Mechanisms of Atrial Electrical Remodeling (AER)
http://my.clevelandclinic.org/heart/atrial_fibrillation/AFresearch.aspx#atrial_electrical

where they discuss the roll of calcium ions and calcium overload in the context of AF.
So what is the connection with a cardio-selective beta-blocker? In Klaubunde's cvpharmacoly one can get more knowledge.
http://cvpharmacology.com/cardioinhibitory/beta-blockers.htm
I the section with heading Heart it is explained how the beta-adrenoceptors works and in particular the bete1 receptor. Note that the end game is that calcium-ions are released inside the heart cell, partially from influx trough the cell membrane but also from the inside reservoir, sarcoplamic reticulum. The released Ca-ions then are directly responsible for the cell contraction. By taking a beta1 selective beta-blocker this activity is reduced and my hypothesis is that use of a beta1 selective beta blocker the surplus of Ca-ions is not getting bigger than that the normal Ca-pumps can take care of it and even turn-around an from earlier attacks acquired calcium overload.
As we are in that area, I cannot help but also give the link to digoxin:

http://www.cvpharmacology.com/cardiostimulatory/digitalis.htm
Digoxin works: “By inhibiting the Na+/K+-ATPase, cardiac glycosides cause intracellular sodium concentration to increase. This then leads to an accumulation of intracellular calcium via the Na+-Ca++ exchange system. In the heart, increased intracellular calcium causes more calcium to be released by the sarcoplasmic reticulum, thereby making more calcium available to bind to troponin-C, which increases contractility (inotropy). Inhibition of the Na+/K+-ATPase in vascular smooth muscle causes depolarization, which causes smooth muscle contraction and vasoconstriction.
By mechanisms that are not fully understood, digitalis compounds also increase vagal efferent activity to the heart. This parasympathomimetic action of digitalis reduces sinoatrial firing rate (decreases heart rate; negative chronotropy) and reduces conduction velocity of electrical impulses through the atrioventricular node (negative dromotropy). “
I think it is time to ask what kind of connection a cardiolog has to the department that performs the ablation or ablate the AV node and inserts a pacemaker. Is there possibly a case of kickbacks? The only exception would be a little ol’lady with AF at a too high heart rate and with a blood pressure that does not allow the use of a beta-blocker, but then you are not talking about a cure for AF, instead it is about life saving.
At the same page the Na+-Ca++ exchanger is described. When the influx of Ca++ ions is larger than the exchanger’s capacity, a Ca++ overload will start to form.
More about Ca removal is said at:
http://www.cvphysiology.com/Cardiac%20Function/CF023.htm
My hypothesis is supported by these experiments and there are others:
http://www.ionchannels.org/showabstract.php?pmid=8653882
The highly beta1 selective beta-blockers were not available at the time these experiments were done and verapamil at a concentration needed to stop calcium overload possibly could have too strong side-effects to be useful in humans. Time to repeat these experiments with Bisoprolol instead.

6
When AF stops I do not take any more beta-blocker, but it is very important to take half-a pill 2-3 days afterwards to counter the body’s reaction to the lack of beta-blocking. If not so an adrenergic AF attack will follow. The abstinence can be seen as a rise of the systolic blood pressure. It is too easy to get into a cycle with 2 attacks/week, if not this precaution is followed.
End of Gunnar’s protocol

I am a believer that you should follow the money stream. Therefore I am rather pessimistic about research in the field I have described above. The ablation industry is extremely lucrative. From the device manufacturer, over the hospitals and the EPs performing ablations. That is why I do not think the EPs that George mentioned would have any interest. They are extremely good at ablate failing hearts and let us continue them to do so. Why should they have an interest to even make a little dent into the branch they are sitting on? The most interested would be afibbers and those who pay the bills, the insurance companies. I am now thinking of the US. There might be a never ending supply of AF-patients that want an ablation, but there is a limitation on how much many that can be allocated for the task. The financial crisis really highlighted that problem. Think of the Big Three and the health reform. In Sweden personal at the hospitals are reduced. Even nurses. The staff at the cardiac department of my own hospital was reduced by 12 individuals. The cost for care of AF patients is around SEK 6 billions in Sweden. 6000 new cases are added to the 300.000 at hand every year at and that number is increasing as the population gets older. The number of ablations per year is about 1200. The cost for an ablation is well over SEK 100 000. The only possible solution that can make a difference is pharmacological. The patents on most drugs that are used have expired and the generics are cheap.
I think the statistics I have presented are quite unique if you see to the period of time they represents. Changes take time before they can be noticed and the data are scattered. Look at the time for conversion. It varies a lot and I know about it. Everything feels OK for a conversion, the heart rate is well under 100 and I cannot feel the heart beats, the time is in from previous experience. Still it does not happen. At situation like that I take a hot bath or a 20 min. walk and than I convert. But it is not always possible to do that to get the shortest AF event as possible. You might be to tired after a night with little sleep and when the heart quits down you just have to take a nap first etc.

I will make the program available later in April to be mailed to post addresses outside the US at a price of USD 250 paid through a PayPal account that I right now do not have. I have written the program with the priority to help to cure my AF, not to start a business, but the experience I have got from having this resource, is so advantageous that I want to share it with other afibbers. I am an afibber not a businessman in the IT-industry. Without it, how do you know that your drugs or for that matter your supplements help? Changes are so slow and there is simply not enough time to make that kind of statistics manually. My intentions at the start was to make something that handled my drug intake

when I got an attack, but after hand I have also included the task of making something that also would reduce or stop the AF. Thanks for reading.

Gunnar

Here is an article about ß-Adrenergic Stimulation Modulates Ryanodine Receptor Ca2+ Release During Diastolic Depolarization to Accelerate Pacemaker Activity in Rabbit Sinoatrial Nodal Cells

http://circres.ahajournals.org/cgi/reprint/90/1/73

That supports my hypothesis that it is the heart selective beta-blocker that reduces the accumulation of Ca++ overload when in AF. It seems to be a matter of Ca++ induced Ca++ release by ryanodine receptors from the sarcoplasmic reticulum in the cardiac myocyte.

Gunnar

I have embedded the Excel charts into the program, so there is now no need to run Excel to see them. See picture 15.

Gunnar

I was offered a Maze procedure in January 2008 by the Public Health system. I the fall of 2007 I made preparations to have an ablation in Denmark. I did not follow up on either as my AF-attacks became less frequent to a total stop 2007-12-28 to 2008-12-23.
I have tried Taurine 3 times with the same result: I get bigemini for more than 20 hours, which I find worse than AF as the effective pulse rate is about 32.

My potassium lies within the normal range. If potassium supplementation should have any effect for a person that is within normal range of potassium serum concentration you need to be at the upper limit or just pass it to achieve a prolonging of the Effective Refractory Period in phase 3 and 4 to stop the arrhythmia. By pushing the envelope with potassium supplementation the serum concentration will rise and reduce the potassium concentration gradient so conduction through the ion-channel gets slower. The potassium blockers like sotalol, tikosyn, amiodarone etc partially inhibits the outflow of potassium-ions. The result is equal for both methods: prolonging of the ERP.
http://cvpharmacology.com/antiarrhy/potassium-blockers.htm

I feel safer to use Sotalol and achieve this prolongation under more controlled circumstances by letting the program calculate "levels" and for a stretched out period of flimmer get an EKG to check the QT/QTc valued. To take a pill is also a more exact measure of the amount than using a supplement.
The software in modern EKG monitors cannot distinguish an overdose of a potassium blocker with hyperkalemia. Both give the same flattening and prolongation of the T-wave.
http://en.wikipedia.org/wiki/Hyperkalemia

Gunnar

I have been thinking in the same lines as you about placing the PiP-generator on a server, but you really want the statistics from the database also.
Putting everything on a server is outside my scope. Remember I have written the software to help myself to reduce the effects of AF. I do not have the money, perhaps a million to write the software, sell it to hospitals and train staff. It is totally outside my scoop. My idea has not been to provide the medical society with a new tool to make money. I agree to that the software package is not for everyone, but many of the baby-boomers, who now are entering the AF-age are absolutely capable for the task. They will get the "levels" from their physician and feed the program with date and time and I am sure they will handle the prescription drugs with the same respect as they do today. In that regard there is really no difference. I also think it is a good idea to give the patient more responsibility for their own well being than favour a behavior to put the total responsibility on another party, the physician and for future cost reasons I think that is necessary.

Again, remember my driving force is to get rid of my AF not to get into the news.

Gunnar

I have sent e-mail with a link to my website to several "Heart Associations". Also organizations that supply the money would be a good target, e.g. insurance companies. I have asked for their help to get the Sotalol-Bisoprolol tested clinically.

If an afibber is interested in my protocol he could ask his physician. It would be a good idea to bring a piece of paper to the physician with the URL written down: http://hem/bredband.net/fibrillations/

Even if many physician refuse to listen to treatment ideas from their patients I think many would be curious enough to, when time allows, to look at the page. You do not need the software to test the protocol. I have used it from 2005 without any computer support.

The program can already be used to transfer data between the afibber and his physician. If the afibber burns a copy of the database on a CD and bring that with him to the physician. Everything is accessible on the physicians computer by getting into Settings and change the location and name on the current database. All screens and printouts will also have the afibbers name and ID-number at the top. I blanked those fields in the screen shots at my webpage.

Gunnar

For those interested in a deeper understanding of Ca++ overload:
http://books.google.se/books?id=o4iLFX67P3kC&pg=PA103&lpg=PA103&dq=atrial+fibrillation+caLCIUM+OVERLoad&source=bl&ots=T3SKjZJsxj&sig=MFd9FKhxMaHn6W_r4p44rVQ0baQ&hl=sv&ei=MpvLScy1Ms3R-Qb3-8y6Bg&sa=X&oi=book_result&resnum=3&ct=result#v=onepage&q=atrial%20fibrillation%20caLCIUM%20OVERLoad&f=false

Gunnar

I have enhanced the screen as seen in Picture 4, Time Past, to include a chart and a table. With this screen you can see how the fall out would be in the chart, if you have a new AF-Event at a certain date and time. In Picture 16 you can see if you get under or over the trendline, if you would have an Event in this case April 9 at 22:23. As long as the trendline is going upwards you are prolonging the AF free time between events. By default the calculations start 1 year back. I only have data from 2009-06-13.

Gunnar

THE AFIB REPORT is published 10 times a year by:
Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: editor@afibbers.org World Wide Web: http://www.afibbers.org