Apheresis for Elevated Lipoprotein(a) in the US: a Nationwide Survey of Apheresis Centers in the United States

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A 501(c)3 US tax exempt Public Charity
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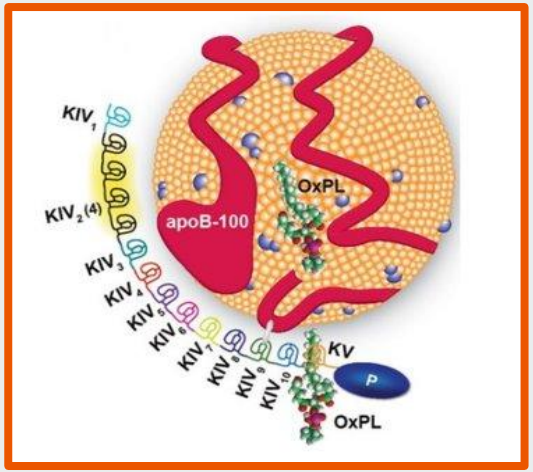


Apheresis Use in Europe, UK and Russia

Apheresis is utilized for treatment of patients who have elevated Lipoprotein(a) {Lp(a)} with Coronary Artery Disease (CAD), and is commonly employed in Germany, other European countries, Russia and the UK. Literature indicates that 1,500 patients receive this treatment in Germany alone. In the United States (US), apheresis use is thought to be low, but there is no known study looking into this.

Methods to identify all apheresis Centers In US

To determine the total number of patients receiving apheresis for elevated Lp(a) {Hyperlipoproteinemia(a)} with advanced CAD in the US, all apheresis centers in the US were first identified The FH Foundation Registry of US apheresis centers was first consulted. The accuracy and comprehensiveness of this Registry was determined using a list of Liposorbers maintained by Kaneka Pharma of America. Kaneka is the only company providing apheresis equipment in the US.

Method of Survey

The medical director of each site was initially contacted via e-mail. If no initial response another e-mail was addressed to medical director. In addition individual e-mails were sent to other team members including registered nurses, technicians, and administrators.

If still no response phone calls were made until the site was reached. Of concern was that two of the medical directors contacted by phone were not aware that apheresis could be used for treatment of elevated Lp(a).

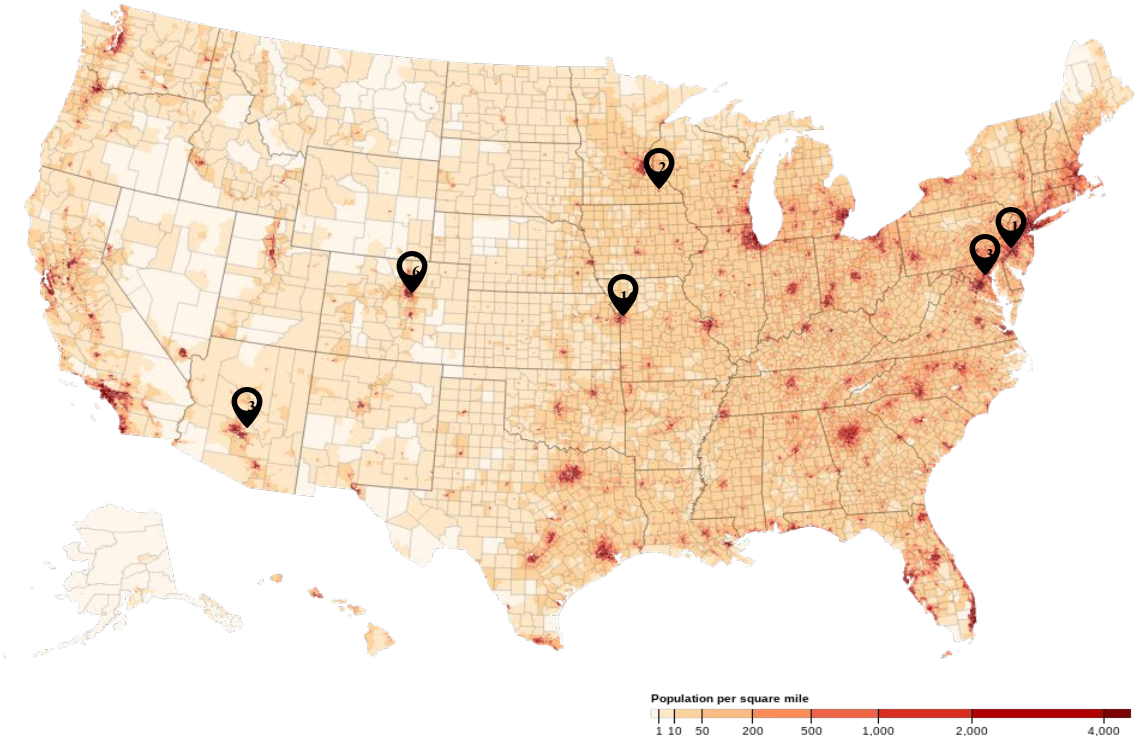
Only 31 patients receive apheresis for Lp(a) in the entire United States

Thirty-one patients receive apheresis for Hyperlipoproteinemia(a) { elevated Lp(a) }with advanced CAD in the US at the present time. The literature indicates that in Germany 1,500 patients are treated with apheresis for Lp(a) with CAD.

The criteria required for treatment is the same in both countries. Both countries' populations have similar rates of people and similar levels and distribution of Lp(a) complicated by advanced CAD.

All Apheresis Centers in the United States treating patients exclusively for Lp(a)

In the United States there are only 6 centers treating patients exclusively for elevated Lipoprotein(a). These centers have a combined total of only 31 patients.



300-fold difference in rates of Lp(a) apheresis

The indications for treatment and the percentage of the population with elevated Lp(a) patients are very similar in Germany and the US. This allows the calculation of the number of patients that should be treated in the US.

The population difference of 360 M in US vs 60 M in Germany results in a factor of 6. The estimate of patients receiving apheresis for just elevated Lp(a) and advanced CAD is approximately 1500 patients in Germany. This means that approximately 9,000 patients should receive Lp(a) Apheresis for just elevated Lp(a) and advanced CAD in the US. This comprehensive study found only 31 patients being treated in the entire US. This represents an unfortunate 300-fold difference.

The 300 fold difference is the “tip of the iceberg of the neglect” of Lp(a) in the US

This unfortunate discrepancy is the “tip of the iceberg of the neglect” of a serious public health problem of elevated Lp(a)in the US. The well established fact that elevated Lp(a) independently can cause significant and accelerated coronary artery disease is not accepted.

This is evidenced by the finding that only 1 of 50 practicing health care providers in the US have even heard of the term Lipoprotein(a) or “Lp(a)”.

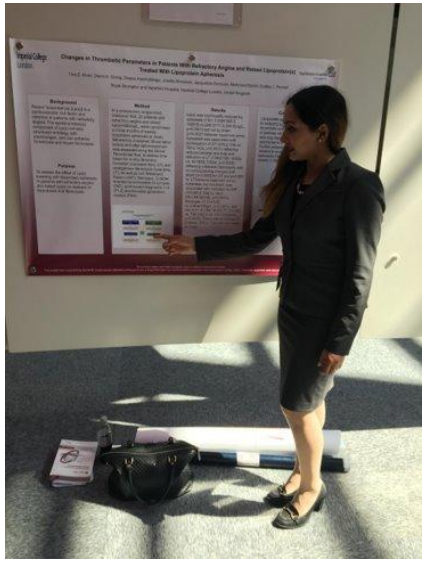
Barriers

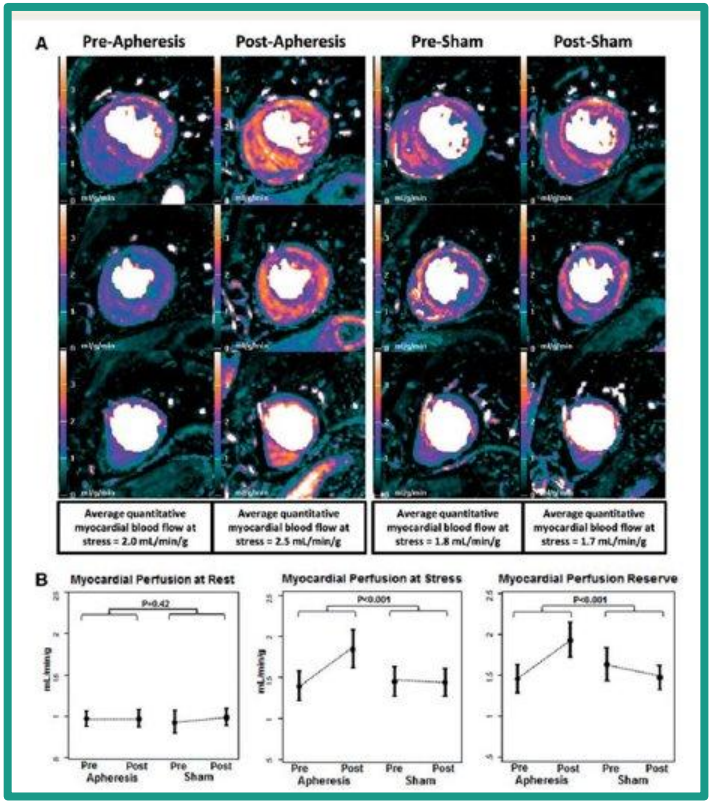
The work of Tina Kahn and the German Pro(a)LiFe Study Group are not published in any widely read US medical journals. The Clinicians practicing in the US are not aware of these important studies.

In Germany it is considered unethical to not treat with apheresis if the criteria are met, which make this knowledge gap very concerning.

Tina Kahn Study

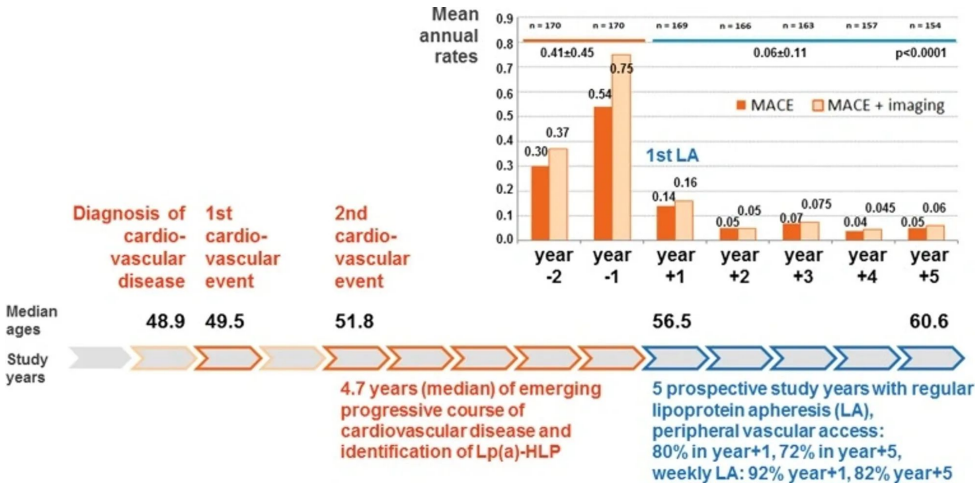
The study is a blinded sham cross over study of Apheresis for advanced CAD with refractory angina. The results were highly significant with a p <0.001 favoring apheresis vs sham procedure. The results can easily seen in the MRI perfusion study.





European Heart Journal (2017) 38, 1561-1569

Cardiovascular Complications Decreased by Lp(a) Apheresis



This study provides strong evidence of the success of weekly apheresis for elevated Lp(a) >60mg/dL and advanced and refractory MACE. Undiagnosed patients served as their own controls. Rates of MACE and MACE + imaging were compared in the two years before apheresis was instituted to the rates during the 5 years after treatment was stated.

Clin Res Cardio Suppl (2017) (Suppl)12:38-43

Health care system has many barriers:

- **Exorbitant High Charges by Institutions**
- **Medicare and private insurers do not reimburse**
- **FDA has not approved apheresis for Lp(a)**

Charges submitted for fortnightly apheresis are often above $250K which is 5 times the actual cost. Medicare and private insurers seldom approve or pay for this treatment. Although Apheresis for LDL is approved by the FDA, the use of the same procedure for Lp(a) is not approved

Guidelines to test Lp(a) levels are not followed

Indications for testing of Lp(a) in the US as recommended by the National Lipid Association are essentially the same as those of the European Society of Cardiology.

However levels are very seldom determined even though indications are very similar to those of ESC. One 350 bed medical center with 75,000 emergency department visits/year and 14 cardiologists had only one test for Lp(a) ordered in 18 months.

Treatment with Statins is the accepted practice and apheresis is not felt necessary

Even if testing is performed the appropriate therapy is not chosen.

It was known at the time statins were introduced that many statins had been found to raise levels.

A WARNING in prescribing information in all of the statins sold was required starting in 2003 in Canada. This WARNING indicated that a statin would not be effective in patients with increased Lp(a) levels. This implied the need for Lp(a) level testing in patients receiving or starting statins. This WARNING was not required in the US even though the same statins and companies were involved.

Now sub analyses of large RCT's have shown that statins are not effective

Unfortunately a single study in 1995 of only 146 patients suggesting that statins by lowering "LDL-C" might reduce risk of MACE in patients with elevated Lp(a) (1) Despite the study being being of only a few patients, extremely underpowered and not confirmed, it was widely used to justify statin treatment.

Two sub-analyses of large, well designed RCT's have refuted this earlier study. Both the sub analyses of JUPITER (2)& AIM-HIGH (3) Trials provide evidence that statins do not reduce MACE events in patients with elevated Lp(a) Practicing health care workers are seldom aware of these studies or do not accept the results. Even if an elevated Lp(a) level is found on testing the problem is not treated correctly. (1) JAMA. 1995; 274: 1771-1774. (2)Circulation, 2014;129:635-642. (3) J Am Coll Cardiol. 2013 October 22; 62(17): 1575-1579.

Niacin despite RCT's not showing effectiveness is used in the US for elevated Lp(a)

Two large well designed RCT's have not supported the effectiveness of Niacin in treatment of patients with elevated Lp(a). These are then AIM-HIGH (1) and the HPS-2 THRIVE (2) that give confirmatory results.

Niacin is known to lower Lp(a) Levels by approximately 30% but this not not result in any favorable effect of clinical outcomes. It is becoming clear that how the medication raises the lipoprotein may determine it's clinically effectiveness. This was demonstrated in studies of CETP inhibitor when very significant elevations of HDL-C only translated small improvements in outcomes. (3) Clinical effectiveness must always be the true test of a new medication or treatment.

(**1**) J Am Coll Cardiol. 2013 October 22; 62(17): 1575-1579. (2) N Eng J Med. 2014;371:203-212. (3) N Engl J Med 2017; 377:1217-1227.

Lp(a) should be called the “apo(a) Lipoprotein” It is truly the “ UGLY” Lipoprotein!

The Mexican Stand off is now complete: The GOOD HDL, the BAD LDL and the UGLY Lipoprotein(a).

It should be separately measured universally and whenever a lipid “panel” is ordered.

Mandatory testing in all individuals is now paramount and an appropriate immediate goal for the EAS, ESC and NLA.

Call to action to help the “neglect” of Lp(a) in US

The United States needs the help of the scientists and physicians in the rest of the world. Please educate your US colleagues and publish in American journals such as NEJM that are read by health care workers that provide primary care and treatment.

Please communicate other thoughts and suggestions to the presenter and the Lp(a)CARE foundation.

Contact Christian G. Schrock cgschrock@gmail.com or lipoproteinacare@gmail.com. Text/voice +1 763-486-0377 or WhatsApp. The Foundation website is Lpacare.com.

Please take a data stick that contains the video presentation of the poster by the Presenter and Powerpoints on Lp(a).

END