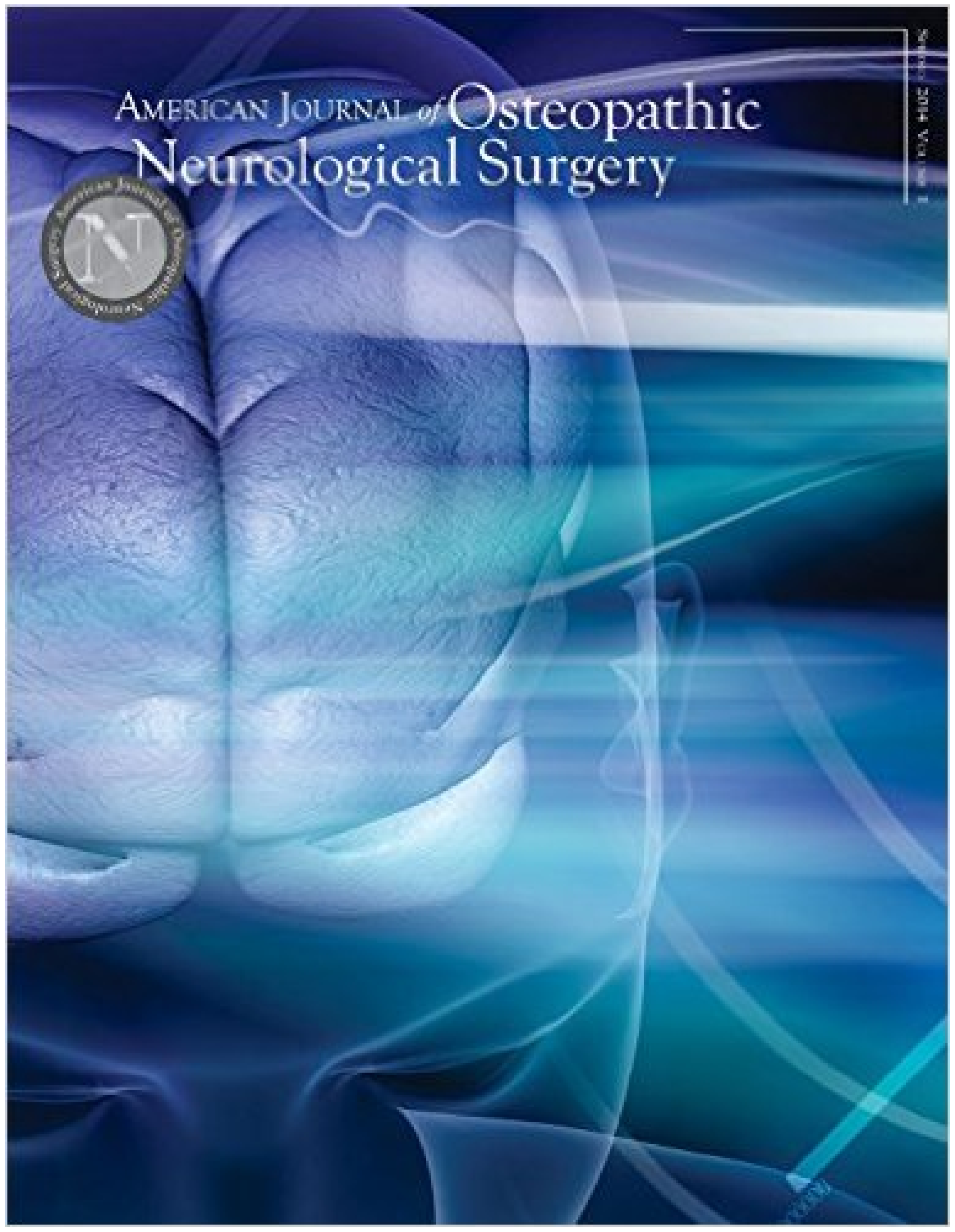
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Papers submitted should be original documentation, including photographs. The papers should be single column, double-spaced in WORD format. The title should be in title case and bold, followed by Authors, degree, organization and city, state.

The papers should contain an abstract and be separated into sections with bold typing of the section title. The page set-up should be 0-6.5 inches. Paragraphs should be indented 0.5 inches. All tables should be submitted separate from the paper. If possible make the tables up to 3 inches wide so that they could fit into a column. This will allow quicker scanning and preparation.

References should be numbered, tab, name of authors, title of paper, journal, year volume:pages.

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EDITOR'S PAGE

Physicians in training, learn and practice research "To formulate, ingrain, and measure, a method of thought, investigation, and evaluation necessary for physicians to have multi-lateral information exchange and communication with experts in areas of scientific and medical discovery, knowledge, and analysis, in order to continuously and efficiently improve human health and patient care." Understanding and performing quality research provides students and residents the tools to propel quality medical care into the community and into the future.

Welcome to the American Journal of Osteopathic Neurological Surgery and the American College of Osteopathic Surgeons Neurosurgical Discipline. This volume is composed of the Residents' annual papers that were submitted but not published elsewhere. It is therefore dedicated to the future Neurosurgeons and their education. All papers were reviewed by the peer review committee and selected for awards. The papers submitted are excellent, representing some of our talented colleagues. Issues will be published quarterly. I hope that this issue will spread the knowledge of our residents and our section. We will continue to solicit annual papers and all papers submitted at the annual meeting. This is your Journal paid for by your annual dues. This issue is available on our website AOANeurosurgery.org. This is your organization; please support it as you can.

Thank you,

Dan Miulli, D.O, F.A.C.O.S
Co-Editor In Chief

2015 Annual Resident Papers Awards

Congratulations on your submission for the 2015 Annual Resident Paper Contest. The winning papers will prepare a 20 minute presentation for the ACOS ACA in Chicago on Sunday October 4, 2015 at 2:00 AM in Chicago Ballroom A/B/C

1st Place Joseph Georges, DO, Use of a Conformational Switching Aptamer for Rapid and Specific Ex Vivo Identification of Central Nervous System Lymphoma in a Xenograft Model

2nd Place Mark Krel, DO, Intraparenchymal Hemorrhagic Stroke Size is Minimal Within an Optimal Range of Total Cholesterol

3rd Place Omid Hariri, DO, Anti-epileptic prophylaxis in traumatic brain injury: A retrospective analysis of patients undergoing craniotomy versus decompressive craniectomy

First place receives $1500.00; Second Place $1000.00; and Third Place $500.00.

ACOS NSD Annual Paper Contest Judging Criteria
The papers judged the best will be original prospective studies in neurosurgery. Case studies and review of the literature are significant contributions and should be combined with retrospective or prospective procedures to qualify as best papers. Papers will receive up to 100 points in each category for a total of 500 points. The categories judged are: 1. Type of Research Paper (basic science, original clinical research, prospective study, chart review, review of literature, case study), 2. Grammar, 3. Addition to Science, 4. Research Conducted, and 5. Change to Neuroscience Practice.

Intraparenchymal Hemorrhagic Stroke Size is Minimal Within an Optimal Range of Total Cholesterol

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Abstract

Background and Purpose: Risk factors for intraparenchymal hemorrhages (IPH) include total cholesterol (TC) above 200, and yet a severely decreased level of TC interferes with the stabilization of the cell membrane and can lead to a larger hemorrhage. This study looks for the optimal range to limit hemorrhage size.

Methods: 229 adult patients with ICD-9 code for hemorrhagic stroke, from June 2007-June 2013 were retrospectively reviewed. Data collected included NIH Stroke Scale, Total Cholesterol Level, Triglyceride Level, LDL and HDL, cholesterol reducing medications, CT hemorrhage size, hemorrhage location, and patient disposition. Statistical analysis was done using Generalized Linear Modeling with Wald Chi-square statistical determinant.

Results: Hemorrhage size is larger in larger brain areas with minimum bleed size in TC range 176-185. This effect is statistically significant independent of location ($\chi^2(25)=43.079$, $p=0.014$). HDL has a significant independent effect on bleed size ($\chi^2(75)=282.567$, $p < 0.0005$) with minimum occurring with HDL 45-54 mg/dL (35-44 mg/dL men, 65-74 mg/dL women). This sex effect within HDL on hemorrhage size is statistically significant ($\chi^2(17)=53.298$, $p < 0.0005$) as is triglyceride level ($\chi^2(20)=129.22$, $p<0.0005$) with the minimum bleed occurring within 128143 mg/dL. Post-hospital patient disposition was not significantly affected by any of the above predictor variables.

Conclusions: TC, HDL and triglycerides in specific ranges are associated with significantly decreased hemorrhage size across all genders and hemorrhage locations. Hemorrhage -limiting effect are strongest at: TC 176-185 mg/dL, HDL 45-54 mg/dL (35-44 mg/dL for men and 65-74 mg/dL for women), triglycerides 128-143 mg/dL. Lipids above or below these ranges yield larger hemorrhages.

Key words: hemorrhage, cholesterol, statin, triglyceride, risk factor, stroke

Subject Codes: Stroke: [43] Acute cerebral hemorrhage; Treatment: [122] Secondary prevention; Imaging of the brain and arteries: [66] Risk factors for stroke; Imaging of the brain and arteries: [64] Primary and secondary stroke prevention; Imaging of the brain and arteries: [62] Intracerebral hemorrhage.

Introduction:

Stroke is the fourth leading cause of death in the United States. It is also the leading cause of adult disability. There are more than 150,000 stroke deaths per year, more than 795,000 new strokes, and more than 4,400,000 stroke survivors in the US with a projected 65% linear increase in these numbers through 2025[1]. The majority of strokes fall into two categories, ischemic and hemorrhagic2, [3]. Intraparenchymal hemorrhages (IPHs) are the most common type of intracerebral hemorrhagic stroke, and are associated with a higher mortality risk than ischemic strokes3, [4]. An intraparenchymal hemorrhage can have secondary insult effects and cause associated perihematoma edema and can subsequently lead to an increase in intracranial pressure (ICP)[4]. IPH typically occurs in the thalamus, basal ganglia, pons, cerebellum, or cerebral lobe. There are many causes of IPH; one of the main associated risk factors includes high total cholesterol level (TCL) above 2003, 5, 6. Furthermore, it is established that an elevated level of LDL increases cellular oxidative stress leading to vascular endothelial dysfunction and triggering the event cascade that ultimately ends in cardio- or cerebrovascular clinical events[7]. Cholesterol must be transported to and from the cells by lipoprotein carriers since cholesterol is insoluble in the blood. TCL consists of High-density lipoprotein (HDL), Low-density lipoprotein (LDL), triglycerides, and lipoprotein A (Lp(a)) cholesterol. HDL removes cholesterol from the blood and therefore protects against myocardial infarction. LDL transports cholesterol to the end organs and in excess throughout the blood is associated with plaque on the walls of arteries which causes arteries to narrow and potentially clot. Triglycerides are blood borne lipid carrier molecules. Triglycerides, a form of fat made in the liver, in higher levels are often seen with high TCLs (4). Lp(a) cholesterol is a genetic variation of LDL and a high Lp(a) level is a known risk factor for premature development of fat deposits within arteries2, 6, 8.

For people over the age of 18, TCL is considered high if it is greater than 200 mg/dL, and a TCL of less than 200 mg/dl is recommended in order to aid in the prevention of stroke and heart disease[6]. It is commonly accepted that there is a direct correlation between total cholesterol level and risk of cardiovascular and cerebrovascular disease. If TCL is higher than 200 mg/dl, or if HDL is less than 40 mg/dl in men, the risk of stroke and cardiovascular disease could increase3, 5, 6, 9-13. According to the American Heart Association (AHA) a healthy level of HDL may protect against heart attack and stroke, while low levels of HDL (less than 40 mg/dl for men and less than 50 mg/dl for women) have been shown to increase the risk of heart disease6, 9, 13-16. An elevated LDL is also a major risk factor for cardiovascular disease, and studies demonstrate that decreasing LDL helps reduce risk for coronary heart disease3, 5, 6, 9, 10, 13-15.

Cholesterol is required for healthy cells because it stabilizes the cell membrane, thus a severely decreased level of TCL interferes with the integrity of cell membrane5, 6, 10, 11, 13, 17, 18. Therefore, it is possible that at some lower TCLs there is less strength of the cell membrane to counteract the force of an expanding hematoma which can potentially lead to a larger area of IPH. Previous population-based studies have confirmed an association between low TCLs and a high incidence of hemorrhagic stroke3, 5, 9, 12, 13, 17-19**.** There have been no studies to date that attempt to determine an optimal range for TCL in order to prevent cardiovascular disease pathology and intraparenchymal hemorrhagic stroke, while also avoiding interference with the ability of cholesterol to stabilize of the cell membrane thereby decreasing the size of the IPH and improving patient disposition after the stroke11, [13]. Thus, if a total cholesterol level lower than 200 decreases the potential for cardiovascular disease, but an excessively low cholesterol level increases the risk of cellular membrane destabilization, and in the event of IPH, contributes to the expansion of the IPH and the severity of the outcome disposition, there exists a need to define an optimal range of goal blood lipids for patient management.

Purpose of Study:

The main goal of this study was to explore the relationship between cholesterol levels, intraparenchymal hemorrhage size, location of the intraparenchymal hemorrhage, and to find an optimal range for total cholesterol levels that will help decrease size of IPH.

Methods:

A retrospective analysis of patient data was performed for stroke patients prospectively entered into Get with the Guidelines Stroke Registry® for the county hospital. It is the largest county by area in the United States and has a diverse range of social, economic and ethnic groups. The hospital is one of the top two busiest trauma centers and emergency departments in California, as well as a tertiary referral center for many diseases. This study was approved by the Institutional Review Board for Human Subjects.

For the purpose of this study, the Stroke Registry data was obtained for the period of Jun 2007 – June 2013 in order to obtain a list of patients by ICD9 code. From this list, the charts for the patients who experienced IPH were retrospectively evaluated, which yielded 229 study-eligible patients (n=229). The ages of patients ranged from 21 years through 98 years. For each patient, the following data was collected and analyzed from the electronic health record system Meditech (MEDITECH, Westwood, MA): National Institutes of Health Stroke Scale (NIHSS), TCL, LDL, HDL, cholesterol reducing medications, size of hemorrhage on CT of the head, location of hemorrhage, and patient disposition. Aneurysmal and traumatic subarachnoid hemorrhage, as well as purely intraventricular hemorrhage and traumatic intracranial hemorrhages were excluded. The intraventricular component of the intraparenchymal hemorrhage was not included in the estimate of size because of the ability of blood to disperse throughout the fluid unimpeded giving a false overestimate of size.

The NIHSS is a quantifying tool used by healthcare providers. It is an objective way to quantify the damage caused by a stroke. It is composed of 11 sections that can be scored between zero and four. A score of zero indicates normal function of that specific ability, and a score above zero indicates that damage has been done to that ability. All of the individual scores are then summed in order to calculate the patient's total NIHSS score. The minimum possible score is a zero, and the maximum possible score is a 42. This scale is used to help determine appropriate treatment, as well as used to predict patient outcome and serve as a measure of stroke severity[20]. Intraparenchymal hemorrhage sizes were determined using the ABC/2 model. The formula for the ABC/2 method can be explained where 'A' is the largest cross-sectional hemorrhage diameter by CT, 'B' is the largest diameter 90 degrees to 'A' on the same slice, and 'C' is the approximate number of CT slices with IPH, multiplied by the slice thickness which was 0.5cm[21]. The product of 'A,' 'B,' and 'C' is then divided by two in order to approximate the volume of the bleed. Hemorrhages that overlapped in areas of the brain were classified in only the one section that contained the majority of the blood. Lesions that occurred in both the Basal Ganglia and Thalamus were classified as thalamic lesions if the bleed was more extensive in that area relative to its total area. Similarly, lesions that occurred in the lobar and, more specifically, the basal ganglia, were classified as basal ganglia bleeds if more extensive in that area relative to its size.

Since this study sought to define an optimal cholesterol range, cholesterol data was binned to a group of ten cholesterol values. This same binning process was carried out for HDL, LDL and triglycerides for consistency and, again, to guide the determination of a specific optimal range. Data was then analyzed using general linear modeling and Wald Chi-square statistical analysis to determine statistical significance. Four factorial analyses were used for the general linear modeling. These were total cholesterol, sex, location, and all two and three way interactions; HDL, sex, location and all two and three way interactions; LDL, sex, location and all two and three way interactions; and triglycerides, sex, location and all two and three way interactions. Lastly, ANOVA was calculated for bleed size as a predictor of outcome using patient disposition as an outcome proxy. All statistical analysis was done using SPSS version 17 (IBM Inc., Armonk, NY).

Results:

There were 229 patients who met inclusion criteria for the study and who had data available for each variable (LDL, HDL, TC, Bleed Size, Bleed Location, Initial NIH, Sex, and Disposition). Summary descriptive statistics are presented in the table below (Table I).

As seen in Figure I, there exists a roughly M-shaped distribution of mean IPH size with a relative minimum, by calculation, occurring in the 176 – 186 mg/dL total cholesterol range across all bleed locations (see arrow). This is to say that when we discount the location of the hemorrhage and strictly compare bleed sizes by total cholesterol levels, the minimum hemorrhage size occurs

in the aforementioned TC range 176 – 186 mg/dL. Performing the analysis mathematically using a generalized linear model accounting for main effects and all factorial interactions, sex by itself has no main effect ($1^2(1) = 1.462$, $p = 0.227$) on IPH size; location, as expected, is tightly linked with IPH size and has a significant main effect ($1^2(5) = 143.474$, $p < 0.0005$); and total cholesterol, binned by 10 mg/dL increments, is a significant predictor of IPH size ($1^2(25) = 43.079$, $p = 0.014$). The interaction of sex and location does not reach statistical significance ($1^2(4) = 7.680$, $p = 0.104$); the remaining interactions, indicated by * (sex * TC, location * TC, sex * location * TC) are all statistically significant (($1^2(17) = 53.298$, $p < 0.0005$), ($1^2(46) = 140.315$, $p < 0.0005$), and ($1^2(17) = 62.601$, $p < 0.0005$), respectively), which speaks to the magnitude of the statistical effect of total cholesterol.

The next comparison of note is a factorial analysis similar to that above but replacing TC with HDL. This changes the factorial analysis to sex, location, and HDL as factors affecting average IPH size. As before, sex has no significant main effect nor does the interaction of sex and location on IPH size. The remainder of the main effects and interactions, however, do reach statistical significance. HDL is even more tightly statistically linked with bleed size than TC ($1^2(75) = 282.567$, $p < 0.0005$). The remaining interactions (sex * HDL, location * HDL, and sex * location * HDL) are all statistically significant predictors of bleed size (($1^2(24) = 97.278$, $p < 0.0005$), ($\square^2(60) = 313.750$, $p < 0.0005$), and ($\square^2(5) = 17.601$, $p = 0.003$), respectively). Comparing figures 2 and 3, overall, the smallest bleed sizes across all genders and locations occur when the HDL is between 45 and 54 mg/dL. If gender is reintroduced as a factor, an optimum HDL range is observed for men at 35 – 44 mg/dL while the optimal range for women occurs at HDL 65 – 74 mg/dL. This effect, as mentioned previously, reached significance and is quite pronounced in Figure III. It should be noted, that outliers were excluded from this analysis. In this case, outliers occurred at HDL > 85 mg/dL. These were treated as outliers, in most instances, due to the paucity of cases (never more than two patients) at each range of HDL. This effect of HDL * sex on mean IPH size is conserved when location is reintroduced as a factor. Figure IV demonstrates that generally but not significantly, women have smaller hemorrhages than do men, overall women have higher HDLs than do men, and women benefit from a higher HDL when factored by hemorrhage location than men. The minimum bleed size, when location is included in the factorial analysis, in men occurs at HDL 35 – 44 mg/dL while for women, this minimum occurs at 65 – 74 mg/dL.

Serum triglyceride level is a strong and statistically significant predictor of intraparenchymal hemorrhage size ($\square^2(20) = 129.22$, $p < 0.0005$). In the same way as HDL, triglycerides have a very strong effect on bleed size that transcends into any cofactor, this is to say that when serum triglyceride is considered with bleed location and patient sex (triglycerides and sex ($\square^2(9) = 40.891$, $p < 0.0005$; triglycerides and location ($\square^2(25) = 104.51$, $p < 0.0005$)) both interactions are significant. Unfortunately, the three-way interaction of triglycerides * sex * location

significance was incalculable, however, the trend is represented in Figure V with minimum bleed size occurring at triglyceride levels 128 – 143 mg/dL.

Lastly, it is interesting to note that LDL does not show the same significant effect on bleed size as do TC or HDL. LDL has no significant main effect ($\chi^2(21) = 25.211$, $p = 0.238$), and no significant two- or three-way interactions. Additionally, none of the factors considered in the present study (sex, location, TC, HDL, and LDL) nor does any factorial combination of these has any statistically significant predictive value on the outcome measure used in this study which is disposition (home, rehab, other facility, or expired). Table II provides summary statistics for each main effect and interaction. The significant effects are bolded.

Discussion:

The relationship between cholesterol and cardiovascular risk is long-studied. In particular, subtypes of cholesterol, high and low density lipoprotein (HDL and LDL respectively) have known specific end-organ effects. Namely, HDL binds and removes excess cholesterol from cells and tissues, while LDL delivers cholesterol to the end organs and has been associated with atheroma. Excess LDL is known to be a cardiovascular risk factor associated tightly with heart disease and stroke. Another vascular lipid, triglyceride, has been shown to be inversely related to intraparenchymal hemorrhage. The overwhelming majority of literature aiming to determine optimal cholesterol goals is aimed at the prevention of cardiovascular disease or total disease burden and to our knowledge, this is the first study that has attempted to define a set of serum lipid goal ranges to limit the extent of intraparenchymal hemorrhages[1, 3-6, 9, 14, 22-25]. This study used, as its predictive factors, patient sex, location of bleed, total cholesterol level, HDL and LDL levels, and triglyceride level. The results of the present study help to define specific goal ranges for each type of lipid, as well as for total cholesterol for the limitation of expansion of intraparenchymal hemorrhage. This study did not, however, consider any cardiac issues or comorbidities in this analysis and further work will include finer differentiation on these lines.

Considering single main effects, this study did not show a statistical main effect of sex on bleed size ($p = 0.227$). While it may appear, at first, that this disagrees with existing literature, it is important to note that existing literature on sex differences in IPH has considered only occurrence of IPH by sex, not size of IPH by sex. As would be expected, bleed size was significantly predicted by bleed location with smaller brain areas subtending smaller bleeds ($p < 0.0005$). Total cholesterol had a significant main effect on bleed size ($p = 0.014$) with the smallest bleeds, across all bleed locations and patient genders occurring at total cholesterol levels 176 – 186 mg/dL. HDL, a component of total cholesterol, has long been known as the “good cholesterol” and this moniker holds mainly true in this study with smallest bleed sizes occurring at an HDL level 45 – 54 mg/dL, a level that is consistent with current recommendations.

As is expected, women have a generally higher baseline HDL, all other conditions being equal, than do men. This study demonstrates that women, additionally, have a higher HDL level than men at minimal IPH size in each bleed location. Men in this study, if we include all data, without correction for outliers, had minimum bleed sizes in HDL range 95 – 104 mg/dL while women had minimum bleed size at 65 – 74 mg/dL. When the range of interest is corrected by removing outliers selected by HDL ranges containing two or fewer patients, or, in the case of the HDL range of 85 – 94 mg/dL, the third patient in that group had an amphetamine-induced hemorrhage, the optimal HDL range for women remains at 65 – 74 mg/dL while for men, the overall optimal range of HDL becomes 35 – 44 mg/dL. While this study does not address the biochemistry and physiology of this difference, previous literature suggests that HDL levels are increased by serum estrogen and, the protective effects of HDL may be potentiated by circulating estrogen. It is interesting to note, however, that despite the amount of attention that LDL, garners in the cardiovascular literature and clinical recommendations, our study failed to show a significant effect of LDL level on IPH size ($p = 0.238$). This is consistent with the metadata reported by Goldstein (2009) and highlights how complex the interrelationships between serum lipids, cardiovascular disease, and cerebrovascular disease are. There may be many reasons and, in part, may be due to the less well reported effects of LDL namely transport of fat-soluble vitamins and antioxidants to cells. Perhaps these antioxidant and nutritive effects preferentially protect neural and neurovascular structures and this protective effect balances the harmful effects of "bad cholesterol." Of course, this is best left for specific evaluation in future work.

Triglycerides demonstrated a significant main effect with minimum bleed size occurring at 128 – 143 mg/dL ($p < 0.0005$). Of note, in the 250 – 272 mg/dL range of total cholesterol, there is a dramatic increase in bleed size. This is consistent with the ARIC study[3] and the CHS study3, 11 reports that low triglyceride levels were associated with increased risk of IPH and the work of Do[26] that confirms that excessively high triglyceride levels contribute to atherosclerosis and atheroembolic events. Along those lines, it is important to note that this study considers only intraparenchymal hemorrhagic stroke and that risk factors and effect sizes may well be different in ischemic stroke.

When reintroducing other individual factors to consider two-way interactions of predictor variables on IPH size, other interesting effects arise. Where location was independently predictive of bleed size, the interaction of sex and location diminished the effect below the threshold of statistical significance ($p = 0.104$). This speaks to the degree of similarity in bleed size between men and women across all locations, meaning that a basal ganglia bleed in a woman is likely to be of statistically similar size to a basal ganglia bleed in a man. The interaction of sex and total cholesterol retains significance ($p < 0.0005$), as does location and total cholesterol ($p < 0.0005$). This implies that, as noted previously, total cholesterol has a significant main effect on bleed size, and that this effect is different between men and women

with women having somewhat higher total cholesterol levels than men (mean TC for men = 173.51, mean TC for women = 184.35).

The interactions between sex and HDL and location and HDL are likewise statistically significant (both, $p < 0.0005$). As noted previously, the maximally protective HDL level for men is 35 – 44 mg/dL while for women it is 65 – 74 mg/dL. As mentioned above, the reason for increased female HDL level is likely to be related to circulating estrogen levels and a potentiating effect that estrogen may have on vasculoprotective HDL. This difference reverses when location is reintroduced as a factor but that will be discussed after all two-way interactions. Also, of note, as would be expected with the lack of a main effect of LDL on bleed size, no two-way interactions are found to be significant with sex ($p = 0.171$) and location ($p = 0.073$).

Triglycerides, again, show significant two-way interactions with both sex ($p < 0.0005$) and location ($p < 0.0005$). The optimal range of triglycerides producing minimum bleed sizes occurred at 128 – 143 mg/dL. These levels coincide with "high normal" levels in clinical practice. This range producing minimum bleed size was conserved between the sexes and among all locations. It is important to note, however, that men, on average, had higher triglyceride levels than women and that men with triglyceride levels > 289 mg/dL had vastly larger bleed sizes. In this study, very few women had triglycerides that were so elevated, however, those few that did presented with much smaller bleeds than did their male counterparts. Of uncertain clinical value, though important to note, bleeds of patients with "high triglycerides" tended to occur in the basal ganglia with extremely large and catastrophic bleeds at triglyceride levels > 289 mg/dL occurring almost exclusively as lobar bleeds.

Now considering three-way interactions, sex, location, and total cholesterol were statistically significant ($p < 0.0005$). This implies that the optimal range noted previously, 176 – 185 mg/dL of total cholesterol has a strong enough effect that it transcends gender and bleed location. This is to say that across all genders and all bleed locations, this range of total cholesterol will yield minimum bleed sizes. The three way interaction of sex, location, and HDL warrants some further discussion. Above, if the sample is considered with obvious outliers, it was noted that overall, HDL 95 – 104 mg/dL was maximally protective against IPH expansion. This, however, means, that with optimal triglyceride range, 128 – 143 mg/dL, using the formula TC = TG/5 + HDL + LDL, to meet the optimal total cholesterol range of 176 – 185 mg/dL, a patient may only be allowed to have LDL 52 – 55 mg/dL. While this is, of course, impractical, it is also potentially unsafe as LDL is a carrier molecule for fat soluble vitamins and antioxidants. It is therefore crucial to consider the three-way interaction of sex, location and HDL on IPH size. Once location is reintroduced as a factor, men and women demonstrate different patterns of HDL that yield the minimal IPH size, with men having optimal HDL ranging 35 – 44 mg/dL while women occur at 65 – 74 mg/dL. The reasoning behind the specific exclusion of outlier data has been discussed earlier. Furthermore, returning location as a factor in the analysis statistically negates the effect of

that single unusual patient and elucidates real sex-specific optimal ranges of HDL. Furthermore, returning to the TC formula, with the constraints as given above, makes the theoretical optimal LDL range 112 – 115 mg/dL for men and 83 – 86 mg/dL for women or 102 –105 mg/dL overall. These ranges, however, were not statistically significant in the current sample. Again, a treatment of the specific physiology of this difference is outside the scope of this study, but it is likely that estrogen and its effects on cholesterol metabolism play a critical role here.

Conclusion:

This study provides evidence for optimal serum lipid ranges for minimizing intraparenchymal hemorrhage sizes. Current clinical guidelines suggest a total cholesterol level > 200 mg/dL contributes to cardiovascular disease. This study demonstrates that when an IPH occurs, the optimal total cholesterol falls between 176 mg/dL and 185 mg/dL to yield the minimal IPH size. The study was not developed to distinguish the optimal cholesterol that would result in less IPH. The range 176 mg/dL and 185 mg/dL will be neuroprotective in the sense that it will minimize intraparenchymal hemorrhage size when it occurs and falls within the established cardioprotective range of current clinical practice. Furthermore, this study demonstrates the component molecules of total cholesterol, with the exception of LDL, also have particular optimal ranges. HDL is optimized for men at 35 – 44 mg/dL and for women at 65 – 74 mg/dL. Triglycerides are optimized at 128 -143 mg/dL. Of note, each of these ranges, with the exception of HDL that has no established clinical ceiling of normal, falls on the high side of "normal" in currently accepted laboratory ranges. Lastly, having optimal ranges of component molecules as well as a goal range for total cholesterol will allow for tailoring of therapy in patient care to minimize bleed size should one occur and thereby the sequelae.

Disclosures: None

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Table I.

Demographics		
Sex	**Count**	**Percentage**
Male	124	54.15%
Female	105	45.85%
Age		
< 40	15	6.55%
41 - 51	42	18.34%
52 - 62	71	31.00%
63 - 73	41	17.90%
74 - 84	47	20.52%
> 85	13	5.68%
Race		
Asian	12	5.24%
Black	34	14.85%
Hispanic	112	48.91%
White	67	29.26%
Other	4	1.75%
IPH Location		
Basal Ganglia	88	38.43%
Cerebellum	25	10.92%
Lobar	78	34.06%
Pons	9	3.93%
Thalamus	29	12.66%

Table I: Summary demographics and IPH frequencies by location.

Table II.

Main Effects on IPH Size	**p-value**
Sex	0.227
Bleed Location	< 0.000
Total Cholesterol	0.014
HDL	< 0.000
LDL	0.238
Triglycerides	< 0.000
Two-way interactions on IPH Size	
Sex*Location	0.104
Sex*TC	< 0.000
Location*TC	< 0.000
Sex*HDL	< 0.000
Location*HDL	< 0.000
Sex*LDL	0.171
Location*LDL	0.073
Sex*Triglycerides	< 0.000
Location*Triglycerides	< 0.000
Three-way interactions on IPH Size	
Sex*Location*TC	< 0.000
Sex*Location*HDL	0.003
Sex*Location*LDL	0.189
Sex*Location*Triglycerides	--

Table II: Summary table of factorial statistical significance on IPH size. Using an alpha level of 0.05, significant effects are presented in bold.

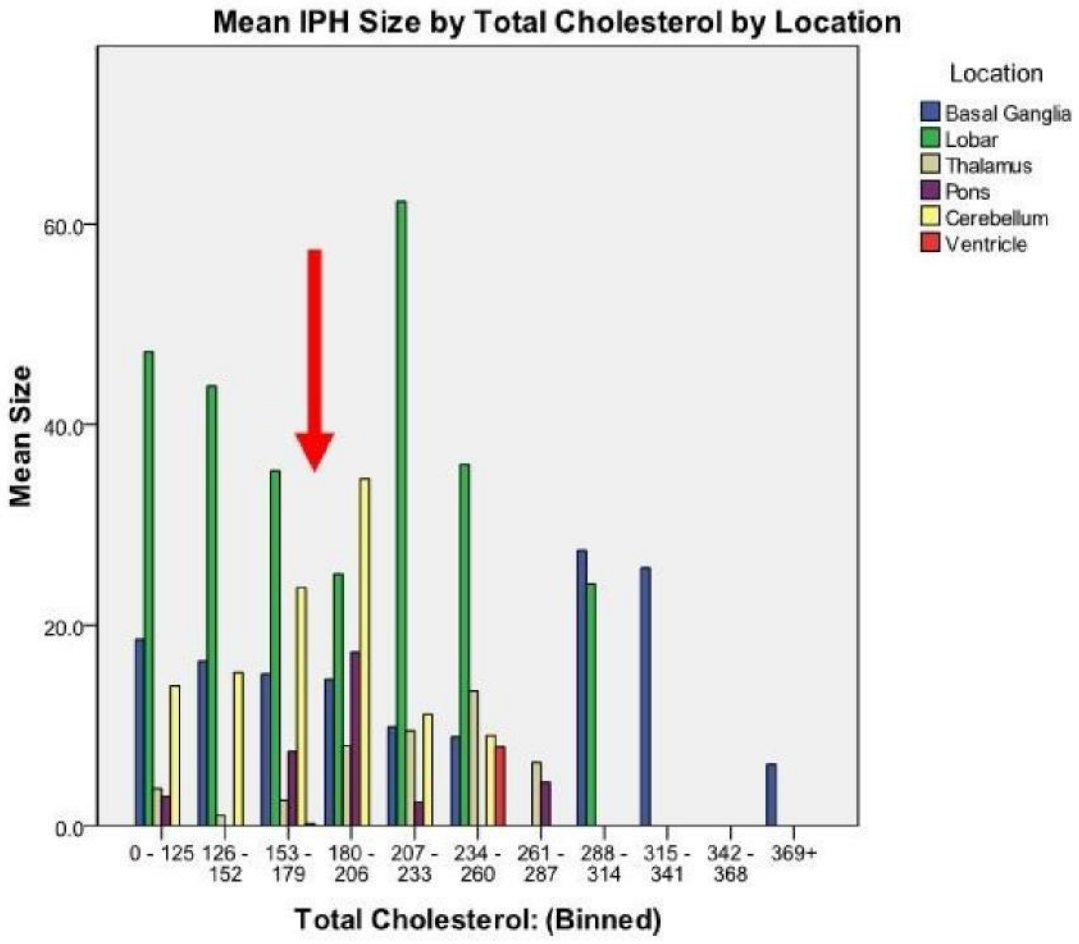


Figure I: Mean IPH Size by Total Cholesterol by Location. As expected, lobar hemorrhages are, on average, larger than other IPH locations. The minimum hemorrhage size occurs with TC between 176 – 185 mg/dL by calculation. In this figure, for the sake of ease of visualization since software constraints would make a graph with bins of 10 mg/dL too dense to read, the graphical bins are larger in width (26 mg/dL) than the computational bins (10 mg/dL). Patients with total cholesterol levels > 314 were very few in number and therefore the patients whose data fall above that TC level were treated as outliers for the computational analysis.

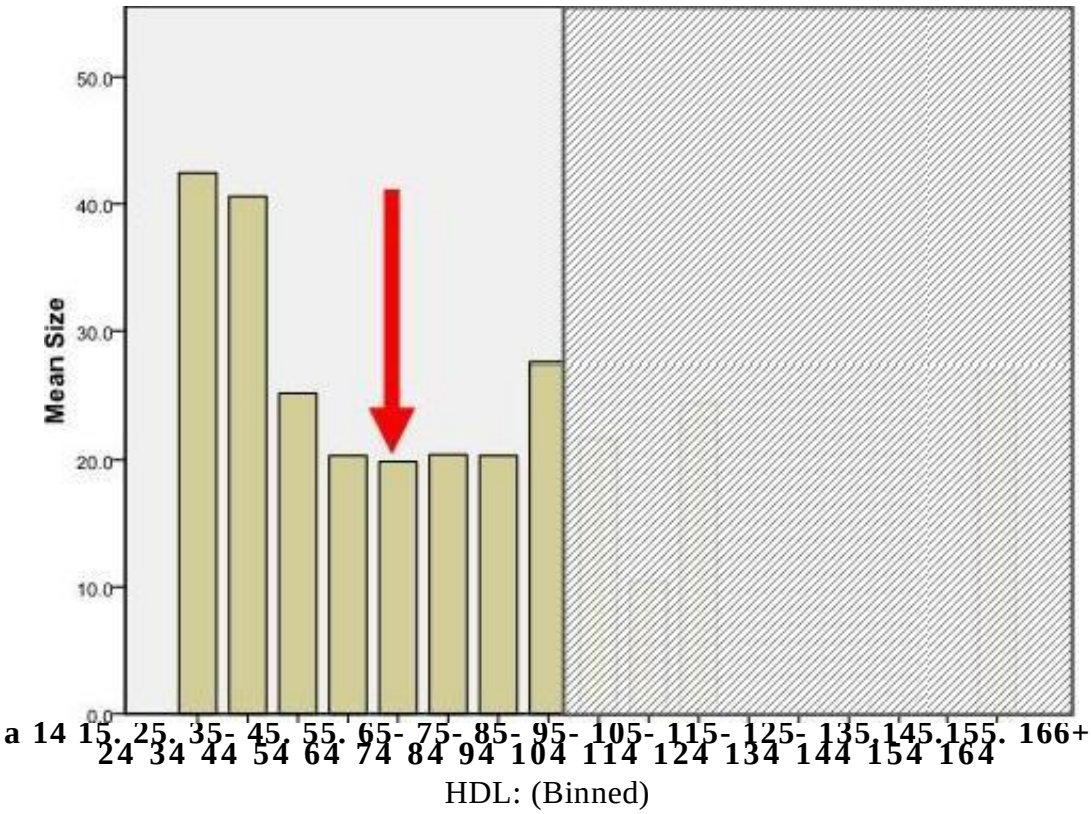


Figure II: Mean IPH size by HDL level. The red arrow indicates the HDL range at which minimum mean IPH size is found (45-54 mg/dL). The shaded region was excluded as outlier data.

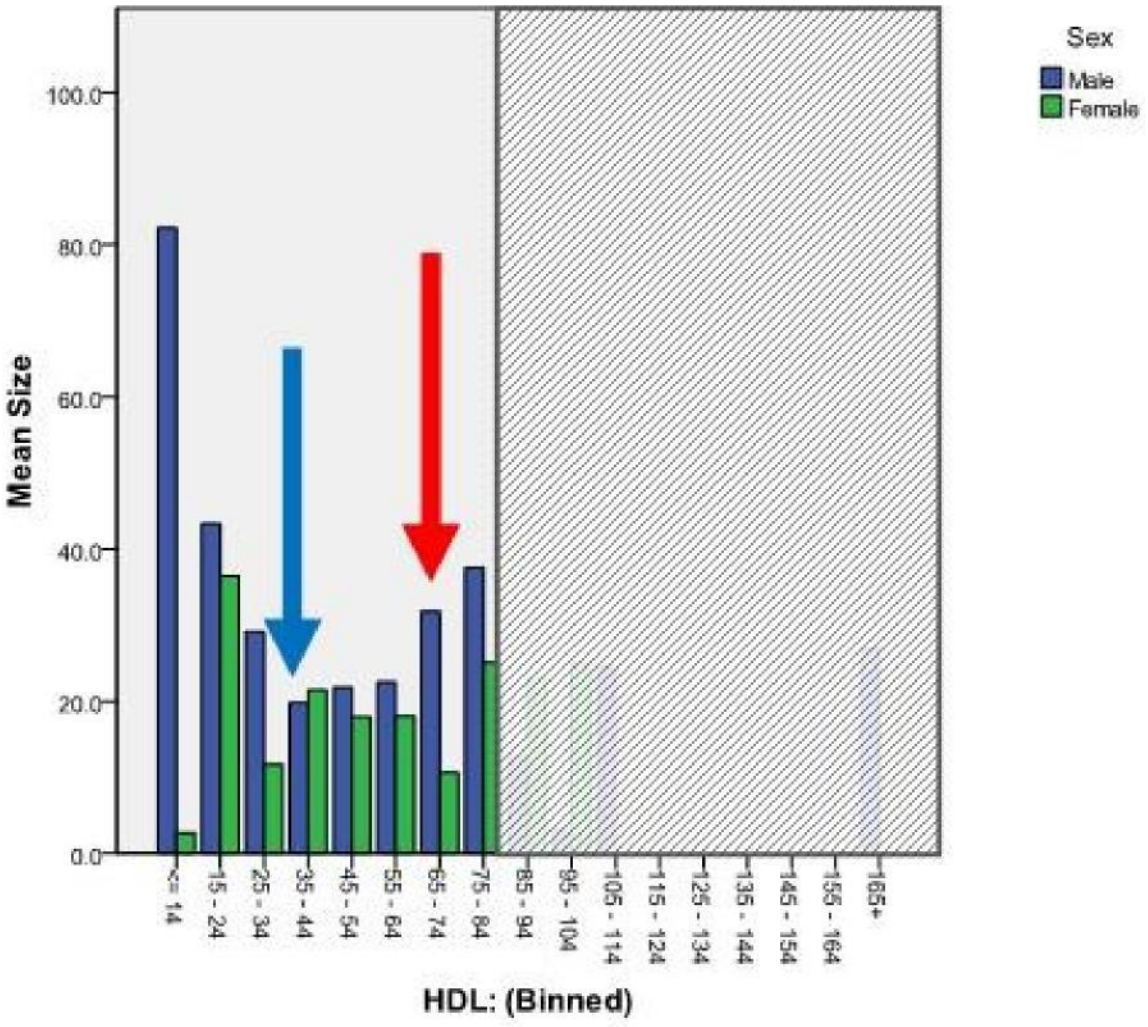
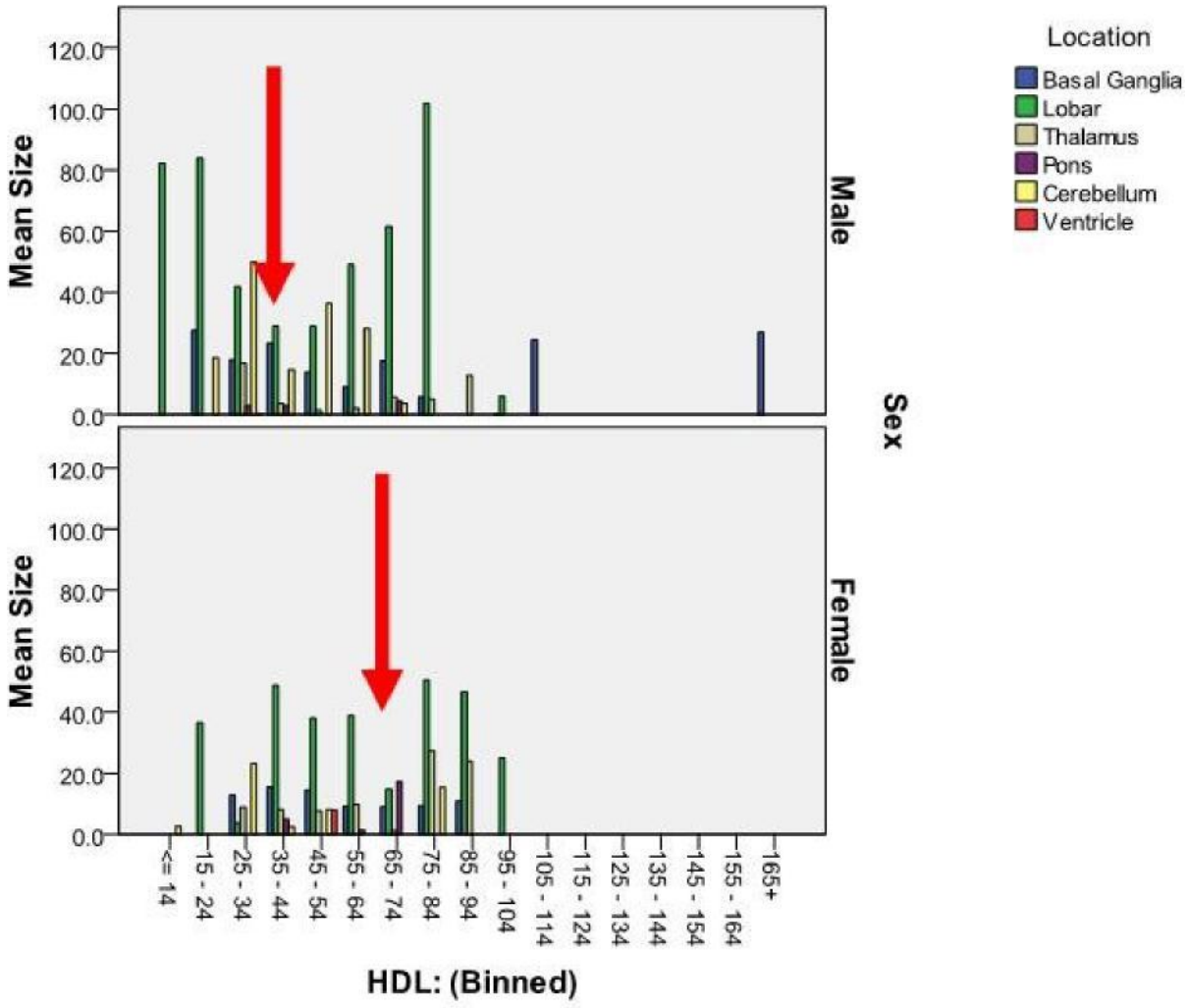


Figure III: Mean IPH size by HDL factoring in gender. Men have minimum bleed sizes across all locations at 35-44 mg/dL and women have the minimum at 65-74 mg/dL. Due to the slight, not statistically significant, male predominance, the overall minimum HDL range occurs as indicated in Figure 2. The shaded region was excluded as outlier data.

Figure IV: IPH size by HDL level, gender, and bleed location. Of note, women have smaller bleeds, higher HDL and seem to benefit from a higher HDL when bleed location is controlled than do men in order to result in smaller IPH.



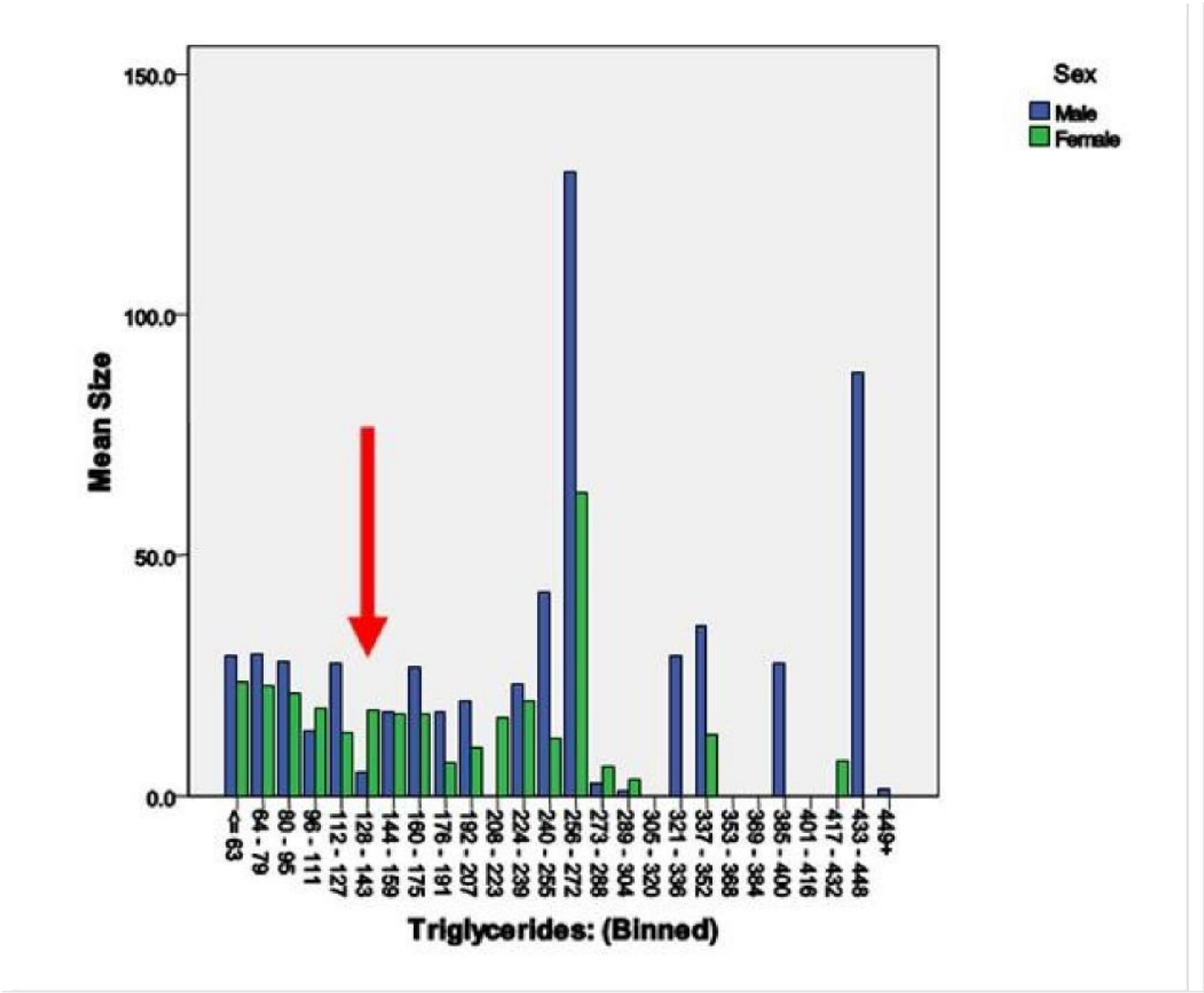


Figure V: Graphical representation of serum triglyceride level by sex affecting mean IPH size. Of note is the huge expansion of bleeds at the 250-272 mg/dL range of triglycerides. The same M-shaped distribution can be seen in this distribution with the minimum bleed size occurring at 128 – 143 mg/dL. Also of note is that of the few patients who had serum triglyceride levels > 289 mg/dL, almost all were male.