Published in final edited form as:
J Vasc Surg. 2014 March ; 59(3): 768–773. doi:10.1016/j.jvs.2013.08.095.

Neutrophil-Lymphocyte Ratio as a Predictor of Cognitive Dysfunction in Carotid Endarterectomy Patients:

NLR & Carotid Endarterectomy

Hadi J. Halazun, MD[1], **Joanna L. Mergeche, BA**[2], **Kaitlin A. Mallon, BA**[2], **E. Sander Connolly, MD**[3,4], and **Eric J. Heyer, MD, PhD**[2,3]

[1]Department of Medicine, Columbia University, New York, NY

[2]Department of Anesthesiology, Columbia University, New York, NY

[3]Department of Neurology, Columbia University, New York, NY

[4]Department of Neurological Surgery, Columbia University, New York, NY

Abstract

Background—Systemic inflammation has been implicated in the development of cognitive dysfunction following carotid endarterectomy (CEA). Neutrophil-lymphocyte ratio (NLR) is a reliable measure of systemic inflammation. We hypothesize that patients with elevated preoperative NLR have increased risk of cognitive dysfunction 1 day after CEA.

Methods—Five hundred fifty-one (551) patients scheduled for CEA were enrolled at Columbia University in New York, NY from 1995 to 2012. NLR was retrospectively reviewed; only 432 patients had preoperative NLR values available within 2 weeks of CEA. NLR was analyzed as a continuous variable and categorically with a cutoff of ≥5 and <5 and equal tertiles, as done in previous studies.

Results—Patients with cognitive dysfunction had significantly higher NLR than those without cognitive dysfunction (4.5±4.0 vs. 3.2±2.6, P<0.001). The incidence of cognitive dysfunction was significantly higher in patients with NLR ≥5 than NLR <5 (34.7% vs. 12.8%, P<0.001). Significantly fewer patients in the low tertile had cognitive dysfunction than in the high tertile (6.9% vs. 25.9%, P<0.001) and middle tertile (6.9% vs. 17.4%, P=0.006). In the final multivariate model, diabetes mellitus (OR: 2.03 [1.08–3.75], P=0.03) and NLR ≥5 (OR: 3.38 [1.81–6.27], P<0.001) were significantly associated with higher odds of cognitive dysfunction, while statin use was significantly associated with lower odds (OR: 0.48 [0.27–0.84], P=0.01).

Conclusions—Preoperative NLR is associated with cognitive dysfunction 1 day after CEA. NLR ≥5 and diabetes mellitus are significantly associated with increased odds of cognitive dysfunction while statin use is significantly associated with decreased odds.

Corresponding Author and Reprint Requests: Eric J. Heyer, M.D., Ph.D., 630, W 168th St, P&S Box 46, New York, NY 10032, Phone: 212-305-9072, Fax: 212-305-8287, ejh3@cumc.columbia.edu.

Attributed Department: Department of Anesthesiology, Columbia University

VII. Funding & Disclosures

No authors have any disclosures to make. Eric J. Heyer, E. Sander Connolly, Joanna L. Mergeche, and Kaitlin A. Mallon were supported in part by a National Institute on Aging grant RO1 AG17604-9.

I. Introduction

Carotid endarterectomy (CEA) reduces the risk of stroke in patients with significant carotid artery stenosis. Although the incidence of stroke during the perioperative period of CEA is 3–5%, a subtler form of neurologic injury, cognitive dysfunction, is exhibited in approximately 25% of patients 1 day after CEA[1, 2]. Cognitive dysfunction has been associated with markers of brain injury[3] and earlier retirement and mortality[4]. While the underlying cause of the cognitive dysfunction is likely multifactorial, previous studies suggest that systemic inflammation plays an important role[5–9]. Systemic inflammation has been implicated in the progression of atherosclerosis and plaque instability[10]. Genetic mutations linked to systemic inflammation[11, 12] and elevated inflammatory markers like monocyte count[6] and monocyte chemoattractant protein[13], are significantly associated with cognitive dysfunction after CEA.

The neutrophil-lymphocyte ratio (NLR) is a readily available marker of systemic inflammation. This ratio is emerging as a robust predictor of deleterious outcomes in many disciplines including, but not limited to, cancer treatment[14–17], coronary intervention[18], coronary artery bypass-grafting[19], and Alzheimer's disease[20]. Some epidemiologic studies show that NLR could actually be a better predictor of coronary syndrome than any other white blood cell count subtype[21, 22]. A 2011 study found that preoperative NLR can identify patients at increased risk of death within 2 years of major vascular surgery and suggested that it could be used as a preventative measure for high-risk patients[14]. NLR has not been directly studied in a population of CEA patients nor has it been investigated for its predictability of cognitive dysfunction. We hypothesize that patients with elevated preoperative NLR have increased risk of cognitive dysfunction 1 day after CEA.

II. Methods

Patients

Five hundred fifty-one (551) CEA patients were initially enrolled with written informed consent in an Institutional Review Board-approved observational single center study at Columbia University Medical Center (CUMC) in New York, NY from 1995 to 2012 (http://www.ClinicalTrials.gov NCT00597883). Eligible patients were scheduled for elective CEA for high-grade carotid artery stenosis (both symptomatic and asymptomatic), English-speaking, and with no axis-I psychiatric disorders. The NLR review was retrospective and therefore, only 432 patients had NLR values obtained 2 weeks before CEA and were the only patients included in this analysis.

Anesthesia & Surgery

All patients received general anesthesia with standard hemodynamic and temperature monitoring, as previously described[1]. None received blood transfusions. The surgical technique, anesthetic management are repeated here [1, 23, 24]. A shunt was available in all cases should EEG changes reflect cerebral ischemia; however, only 9 study patients were shunted intraoperatively based on CUMC criteria for shunting[2].

No patients were premedicated. Patients were sedated with fentanyl and midazolam. General anesthesia was induced with either thiopental, propofol or etomidate. Patients were relaxed with one of the following: succinylcholine, vecuronium or rocuronium. Anesthesia was maintained with muscle relaxation (vecuronium or rocuronium), potent inhalational agent (isoflurane or sevoflurane) with or without nitrous oxide in oxygen (2:1) as tolerated. Standard monitors were applied including an arterial catheter for measuring blood pressure continuously. All hemodynamic data plus temperature were monitored continuously and recorded every minute by a PC-based data acquisition system. Continuous

electroencephalographic (EEG) monitoring was performed on all patients. After cross-clamping the internal carotid artery, a significant EEG change was defined as 50% or greater decrease in amplitude in the alpha or beta frequencies and a similar increase in the delta or theta frequencies, or complete loss of all cerebral electrical activity.

Surgery consisted of positioning the patient supine with the head in an extended midline position. An incision was made along a skin crease from just below the angle of the mandible to near the midline through skin, subcutaneous tissue, and platsyma. The common, internal and external carotid arteries were exposed and controlled. A shunt was prepared and used only if changes consistent with cerebral ischemia were noted on the EEG. After administering heparin intravenously, the common, internal and external carotid arteries were occluded. A longitudinal incision was made in the common carotid artery proximal to the bifurcation and extended into the internal carotid artery distal to the plaque. The atheroma was removed using a dissector. Firmly attached intact intima was left above and below the area of atheroma resection. A patch was inserted for procedures performed by vascular surgeons. The neurosurgeons performed a primary closure. Before placing the final sutures, back-bleeding from the common, internal and external carotid arteries was performed and the lumen washed with heparinized saline. Debris and air were expelled by releasing the clip on the superior thyroid artery, which provided inflow as the final sutures were secured. Clamps were sequentially removed from the external, common and internal carotid arteries."

Neuropsychometric Analysis

The outcome of cognitive dysfunction was evaluated using a battery of neuropsychometric tests preoperatively and 1 day postoperatively. The outcome of cognitive dysfunction is binary (yes/no). The tests evaluate four cognitive domains – verbal memory (Hopkins Verbal Learning Test, Controlled Oral Word Association Test, and/or Buschke Selective Reminding Test), visuo-spatial organization (Rey-Osterrieth Complex Figure Copy and Recall), motor function (Grooved Pegboard and/or Finger Tapping Test), and executive action (Halstead-Reitan Trials A and B). The criteria for cognitive dysfunction are based on difference scores calculated for each test by subtracting the preoperative test performance from the postoperative test performance at 1 day. Similar to previous studies[25, 26], a Z-score was generated based on a surgical reference group's performance to account for practice effect, general anesthesia, trauma of surgery, and the postoperative experience.

The surgical reference group is composed of 156 age- and education-matched patients undergoing lumbar level laminectomy or microdiscectomy ≤2 levels without fusion or blood loss necessitating transfusion. The mean difference score of the reference group was subtracted from the difference score for the CEA patient and then divided by standard deviation (SD) of the reference group ([Difference $_{CEA}$ − Mean Difference $_{Reference}$]/ SD $_{Reference}$). Therefore, each test is evaluated in units of SD of the reference group's change in performance. CEA patient domains were evaluated to account for both focal and global/hemispheric deficits: (1) ≥2SD worse performance in ≥2 cognitive domains or (2) ≥1.5SD worse performance in all 4 cognitive domains. The reference group was only used to generate normalized Z-scores; they were not included in any other analysis.

A variety of factors affect the risk of cognitive dysfunction after CEA. The only ones demonstrated to be significantly associated with the risk of cognitive dysfunction are age >75, diabetes mellitus, and statin use [26–28]. Other factors that may be associated with cognitive dysfunction, but have not been previously published to do so, were evaluated as well. These included sex (male/female), years of education, body mass index (BMI), history of smoking, extensive peripheral vascular disease (PVD), hypertension, symptomatic history of transient ischemic attack or stroke, and duration of cross-clamp of the carotid artery (mins). We have included these all of these factors in our uni- and multi-variate analyses.

NLR

Values from the complete blood count with differential were obtained up to 2 weeks prior to surgery from the hospital laboratory. Most patients had these laboratory tests done as part of their routine preoperative testing. However, only 432 of the initially enrolled 551 patients had NLR data available because complete blood count differentials were not prospectively collected as part of the original study protocol. The 119 patients without NLR in the 2 week time frame either had complete blood counts without a white blood cell differential, had the testing done >2 week prior to surgery, or had the test done at a non-affiliated institution. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count: [neutrophil count]/[lymphocyte count].

Previous studies that have investigated the effect of NLR on clinical outcomes have generally used three methods for categorization of NLR. The first is to treat NLR as a continuous variable and correlate with desired outcome. The second is using an NLR <5 or ≥5 as cutoff values[16, 17, 29]. The third is by categorizing patients into equal tertiles on the basis of their NLR value[30–32]. In this study, we use all three methods of analysis.

Statistical Analyses

Statistical analysis was performed using JMP (SAS Institute Inc., Cary, NC, USA). For univariate analyses, Student's t-test, Wilcoxon rank sums test, Fisher's exact test, Pearson's $\chi 2$ test, and simple logistic regression were used where appropriate. A multiple logistic regression model was constructed to identify independent predictors of cognitive dysfunction. All factors with $P<0.20$ in a simple univariate logistic regression were entered into the final model. Model fit and calibration were confirmed with the likelihood ratio test, Hosmer-Lemeshow goodness-of-fit test, and receiver operating characteristic analysis. In the event of missing values for predictor variables, the sample mean was imputed. $P\leq 0.05$ was considered significant.

III. Results

Patient Characteristics

Patient characteristics were representative of what is expected for CEA patients (Table I). This study evaluated both symptomatic and asymptomatic CEA patients; of the entire cohort, 39.4% (N=170) of patients were classified as symptomatic (Table I). Most characteristics were similar between patients with and without NLR values available. Patients without NLR values available had more hypertension (68.1% vs. 53.5%, P=0.004), statin use (73.1% vs. 57.4%, P=0.002), and longer cross-clamp duration (48.8±17.8 mins vs. 42.9±17.1, P=0.002) than patients with NLR values available (Table I).

Patients with NLR <5 had a mean NLR of 2.4±1.0 while those with an NLR of ≥5 had a mean of 8.0±4.6 (Table II). Patients with an NLR <5 were similar to those with NLR ≥5, with few exceptions; patients with NLR <5 had higher BMI (27.2±4.6 vs. 25.7±3.5, P=0.01) and more statin use (62.8% vs. 30.6%, P<0.001).

Patients in the low NLR tertile had a mean NLR of 1.5±0.4, middle had a mean NLR of 2.6±0.4 and high had a mean NLR of 6.0±3.8. The patient characteristics were similar among the tertiles except for statin use and hypertension, which slightly varied between the low, middle and high tertiles (Table III).

NLR and Cognitive Dysfunction

Of the 432 patients, 16.4% exhibited cognitive dysfunction 1 day after CEA. Patients with cognitive dysfunction had significantly higher NLR levels than patients without cognitive

dysfunction (4.5±4.0 vs. 3.2±2.6, P<0.001). Significantly more patients with NLR ≥5 had cognitive dysfunction than patients with NLR <5 (34.7% vs. 12.8%, P<0.001). Significantly fewer patients in the low tertile had cognitive dysfunction than in the high tertile (6.9% vs. 25.9%, P<0.001) and middle tertile (6.9% vs. 17.4%, P=0.006).

Multivariate Model

Sex, years of education, statin use, diabetes mellitus, and NLR ≥5 were all included in the final multivariate regression model (Table IV). In the final model, diabetes (OR: 2.03 [1.08–3.75], P=0.03) and NLR ≥5 (OR: 3.38 [1.81–6.27], P<0.001) were significantly associated with higher odds of cognitive dysfunction, while statin use was significantly associated with lower odds (OR: 0.48 [0.27–0.84], P=0.01).

IV. Discussion

The NLR is easily obtainable, readily available, and reasonably cost-effective, blood test derived from a complete blood count differential often done as part of preoperative testing. It is a reliable measure of systemic inflammation and has been posited as a predictor of outcomes in a variety of disciplines. However, this study is the first to evaluate NLR in a cohort of patients undergoing CEA and to determine whether NLR is predictive of cognitive dysfunction. Cognitive dysfunction, though less clinically momentous than stroke, has been associated with markers of brain injury[3] and mortality[4].

The most important finding of this study is that NLR ≥5 is associated with a three-fold increased risk of cognitive dysfunction 1 day after CEA. Previous studies have shown NLR's utility in predicting poor outcome following surgery. Gibson et al [19] found that in a cohort of patients undergoing coronary artery bypass grafting, a high preoperative NLR was an independent predictor of poorer survival. Furthermore, Duffy et al [18] show that in patients undergoing percutaneous coronary interventions, an increased pre-procedural NLR is associated with increased risk of long-term morbidity and mortality.

The utility of NLR as a predictive tool extends beyond cardiovascular and cerebrovascular disciplines. K Halazun et al.[17] found that an elevated preoperative NLR prior to liver transplantation for hepatocellular carcinoma significantly increases its risk of recurrence. In their study, an NLR ≥5 is considered to be elevated. We use the same cutoff value, and find that an NLR ≥5 significantly and strongly predicts a poorer outcome following CEA.

Studies have observed that systemic inflammation is detrimental to cognitive functioning, especially in the operative setting[5, 8, 9]. Importantly the relationship between NLR and cognitive decline has been previously demonstrated in a small study by Kuyumcu et al; they found that patients with Alzheimer's disease had elevated NLR as compared to a control population.[20]. The mechanisms of how systemic inflammation and elevated NLR result in cognitive dysfunction remain unclear. Inflammation increases atherosclerotic burden and decreases plaque stability, which may result in increase micro-emboli to the brain. Furthermore, inflammation increases susceptibility to neuronal injury. All these factors place patients with elevated NLR at increase risk for cognitive dysfunction following CEA.

This study also found that diabetes mellitus is also associated with significantly higher odds of developing cognitive dysfunction. This finding is reasonable given that diabetes is considered a chronic inflammatory state and has been previously demonstrated to be a predictor of cognitive dysfunction[27]. It also found that patients taking statins are at significantly lower risk of cognitive dysfunction following CEA. While we did not aim to study this association, it is a potentially interesting relationship that needs further investigation, as we have previously found that statin use is associated with less cognitive

dysfunction in an asymptomatic CEA population[26]. This finding may support the anti-inflammatory properties of statins, but certainly requires further prospective study.

The utility of the NLR as a measure of systemic inflammation prior to CEA is simple, cost-effective, and, most importantly, can provide physicians with an indicator for cognitive dysfunction risk. Further prospective research is necessary to determine whether NLR can be utilized as a preoperative tool to predict and perhaps reduce the incidence of cognitive dysfunction after CEA.

Limitations

We recognize several limitations of this study. First, this was a single center study with retrospectively collected data. As a result, of the 551 patients enrolled in our study, only 432 had NLR data available within the pre-specified time frame of 2 weeks. Furthermore, using NLR in a single preoperative blood sample does not allow for assessing the stability of this variable over time. Additionally, we did not collect data of other inflammatory markers (ie. ESR and C-reactive protein) to determine if it is an NLR specific predictability or that of all inflammatory markers.

V. Conclusion

Preoperative NLR is independently associated with cognitive dysfunction 1 day after CEA. NLR ≥5 and diabetes mellitus are significantly associated with increased risk of cognitive dysfunction. There appears to be an association between statin use and decreased risk of cognitive dysfunction following CEA. Further larger prospective trials are necessary to validate these findings and determine if NLR can be used as a simple predictor of cognitive dysfunction.

Acknowledgments

Hadi J. Halazun, E. Sander Connolly, Eric J. Heyer, Joanna L. Mergeche, and Kaitlin A. Mallon had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Eric J. Heyer, E. Sander Connolly, Joanna L. Mergeche, and Kaitlin A. Mallon were supported in part by a National Institute on Aging grant RO1 AG17604-9.

References

1. Heyer E, Adams D, Todd G, Solomon R, Quest D, Steneck S, et al. Neuropsychometric changes in patients after carotid endarterectomy. Stroke; a journal of cerebral circulation. 1998; 29(6):1110–5.
2. Heyer EJ, Sharma R, Rampersad A, Winfree CJ, Mack WJ, Solomon RA, et al. A controlled prospective study of neuropsychological dysfunction following carotid endarterectomy. Archives of neurology. 2002; 59(2):217–22. [PubMed: 11843692]
3. Connolly ES Jr, Winfree CJ, Rampersad A, Sharma R, Mack WJ, Mocco J, et al. Serum S100B protein levels are correlated with subclinical neurocognitive declines after carotid endarterectomy. Neurosurgery. 2001; 49(5):1076–82. discussion 82–3. [PubMed: 11846900]
4. Steinmetz J, Christensen KB, Lund T, Lohse N, Rasmussen LS. Long-term Consequences of Postoperative Cognitive Dysfunction. Anesthesiology. 2009; 110(3):548–55. [PubMed: 19225398]
5. Kriz J. Inflammation in ischemic brain injury: timing is important. Critical reviews in neurobiology. 2006; 18(1–2):145–57. [PubMed: 17725517]
6. Mocco J, Wilson DA, Ducruet AF, Komotar RJ, Mack WJ, Zurica J, et al. Elevations in preoperative monocyte count predispose to acute neurocognitive decline after carotid endarterectomy for asymptomatic carotid artery stenosis. Stroke; a journal of cerebral circulation. 2006; 37(1):240–2.

7. Heyer E, Mergeche JL, Bruce SS, Connolly ES. Inflammation and Cognitive Dysfunction in Type 2 Diabetic Carotid Endarterectomy Patients. Diabetes Care. 2013; 36:1–4. [PubMed: 23390628]
8. Gorelick PB. Role of inflammation in cognitive impairment: results of observational epidemiological studies and clinical trials. Ann N Y Acad Sci. 2010; 1207:155–62. [PubMed: 20955439]
9. van Harten AE, Scheeren TW, Absalom AR. A review of postoperative cognitive dysfunction and neuroinflammation associated with cardiac surgery and anaesthesia. Anaesthesia. 2012; 67(3):280–93. [PubMed: 22321085]
10. Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation. 2002; 105(9):1135–43. [PubMed: 11877368]
11. Gigante PR, Kotchetkov IS, Kellner CP, Haque R, Ducruet AF, Hwang BY, et al. Polymorphisms in complement component 3 (C3F) and complement factor H (Y402H) increase the risk of postoperative neurocognitive dysfunction following carotid endarterectomy. Journal of neurology, neurosurgery, and psychiatry. 2011; 82(3):247–53.
12. Heyer EJKC, Malone HR, Bruce SS, Mergeche JL, Ward JT, Connolly ES. Complement polymorphisms and cognitive dysfunction after carotid endarterectomy. J Neurosurg. 2013 In Print.
13. Mack WJ, Ducruet AF, Hickman ZL, Zurica J, Starke RM, Garrett MC, et al. Elevation of monocyte chemoattractant protein-1 in patients experiencing neurocognitive decline following carotid endarterectomy. Acta neurochirurgica. 2008; 150(8):779–84. discussion 84. [PubMed: 18574546]
14. Bhutta H, Agha R, Wong J, Tang TY, Wilson YG, Walsh SR. Neutrophil-lymphocyte ratio predicts medium-term survival following elective major vascular surgery: a cross-sectional study. Vascular and endovascular surgery. 2011; 45(3):227–31. [PubMed: 21289130]
15. Sarraf KM, Belcher E, Raevsky E, Nicholson AG, Goldstraw P, Lim E. Neutrophil/lymphocyte ratio and its association with survival after complete resection in non-small cell lung cancer. The Journal of thoracic and cardiovascular surgery. 2009; 137(2):425–8. [PubMed: 19185164]
16. Walsh SR, Cook EJ, Goulder F, Justin TA, Keeling NJ. Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. Journal of surgical oncology. 2005; 91(3):181–4. [PubMed: 16118772]
17. Halazun KJ, Hardy MA, Rana AA, Woodland DCt, Luyten EJ, Mahadev S, et al. Negative impact of neutrophil-lymphocyte ratio on outcome after liver transplantation for hepatocellular carcinoma. Annals of surgery. 2009; 250(1):141–51. [PubMed: 19561458]
18. Duffy BK, Gurm HS, Rajagopal V, Gupta R, Ellis SG, Bhatt DL. Usefulness of an elevated neutrophil to lymphocyte ratio in predicting long-term mortality after percutaneous coronary intervention. The American journal of cardiology. 2006; 97(7):993–6. [PubMed: 16563903]
19. Gibson PH, Croal BL, Cuthbertson BH, Small GR, Ifezulike AI, Gibson G, et al. Preoperative neutrophil-lymphocyte ratio and outcome from coronary artery bypass grafting. American heart journal. 2007; 154(5):995–1002. [PubMed: 17967611]
20. Kuyumcu ME, Yesil Y, Ozturk ZA, Kizilarslanoglu C, Etgul S, Halil M, et al. The evaluation of neutrophil-lymphocyte ratio in Alzheimer's disease. Dementia and geriatric cognitive disorders. 2012; 34(2):69–74. [PubMed: 22922667]
21. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. The American journal of cardiology. 2008; 102(6):653–7. [PubMed: 18773982]
22. Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al. Which white blood cell subtypes predict increased cardiovascular risk? Journal of the American College of Cardiology. 2005; 45(10):1638–43. [PubMed: 15893180]
23. Heyer EJ, Adams DC. Neurologic assessment and cardiac surgery. J Cardiothorac Vasc Anesth. 1996; 10(1):99–103. quiz -4. [PubMed: 8634393]
24. Heyer EJ, DeLaPaz R, Halazun HJ, Rampersad A, Sciacca R, Zurica J, et al. Neuropsychological dysfunction in the absence of structural evidence for cerebral ischemia after uncomplicated carotid endarterectomy. Neurosurgery. 2006; 58(3):474–80. discussion -80. [PubMed: 16528187]

25. Moller JT, Cluitmans P, Rasmussen LS, Houx P, Rasmussen H, Canet J, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. Lancet. 1998; 351(9106):857–61. [PubMed: 9525362]

26. Heyer EJ, Mergeche JL, Bruce SS, Ward JT, Stern Y, Anastasian ZH, et al. Statins reduce neurologic injury in asymptomatic carotid endarterectomy patients. Stroke. 2013; 44(4):1150–2. [PubMed: 23404722]

27. Mocco J, Wilson DA, Komotar RJ, Zurica J, Mack WJ, Halazun HJ, et al. Predictors of Neurocognitive Decline After Carotid Endarterectomy. Neurosurgery. 2006; 58(5):844–50. discussion -50. [PubMed: 16639318]

28. Heyer EJ, Wilson DA, Sahlein DH, Mocco J, Williams SC, Sciacca R, et al. APOE-epsilon4 predisposes to cognitive dysfunction following uncomplicated carotid endarterectomy. Neurology. 2005; 65(11):1759–63. [PubMed: 16207841]

29. Halazun KJ, Aldoori A, Malik HZ, Al-Mukhtar A, Prasad KR, Toogood GJ, et al. Elevated preoperative neutrophil to lymphocyte ratio predicts survival following hepatic resection for colorectal liver metastases. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2008; 34(1):55–60. [PubMed: 17448623]

30. Azab B, Zaher M, Weiserbs KF, Torbey E, Lacossiere K, Gaddam S, et al. Usefulness of neutrophil to lymphocyte ratio in predicting short- and long-term mortality after non-ST-elevation myocardial infarction. The American journal of cardiology. 2010; 106(4):470–6. [PubMed: 20691303]

31. Azab B, Chainani V, Shah N, McGinn JT. Neutrophil-Lymphocyte Ratio as a Predictor of Major Adverse Cardiac Events Among Diabetic Population: A 4-Year Follow-Up Study. Angiology. 2012

32. Azab B, Jaglall N, Atallah JP, Lamet A, Raja-Surya V, Farah B, et al. Neutrophil-lymphocyte ratio as a predictor of adverse outcomes of acute pancreatitis. Pancreatology : official journal of the International Association of Pancreatology. 2011; 11(4):445–52.

Table I

Patients with and without NLR Values*.

	All Patients N=551	With NLR N=432	Without NLR N=119	P†
Age >75	29.6%	28.2%	34.5%	0.19
Sex, male	65.0%	64.1%	68.1%	0.42
BMI, kg/m^2	26.9±4.5	26.9±4.5	27.1±4.3	0.76
Years of Education	14.5±3.3	14.5±3.4	14.5±2.9	0.99
History of Smoking	68.4%	67.8%	70.6%	0.56
Statin Use	60.8%	57.4%	73.1%	0.002
Hypertension	56.6%	53.5%	68.1%	0.004
Diabetes Mellitus	21.1%	20.6%	22.7%	0.62
PVD	29.0%	28.6%	30.3%	0.73
Symptomatic Status	40.7%	39.4%	45.4%	0.24
Cross Clamp Duration, mins	44.2±17.4	42.9±17.1	48.8±17.8	0.002
Cognitive Dysfunction	25.8%	24.3%	31.1%	0.14

* Mean ± standard deviation; BMI – body mass index, PVD – peripheral vascular disease, NLR – neutrophil-lymphocyte ratio

Table II

Patient Characteristics by NLR <5 and ≥5*.

	All Patients N=432	NLR <5 N=360	NLR ≥5 N=72	P†
Age >75	28.2%	28.1%	29.2%	0.85
Sex, male	64.1%	64.7%	61.1%	0.56
BMI, kg/m^2	26.9±4.5	27.2±4.6	25.7±3.5	0.01
Years of Education	14.5±3.4	14.6±3.6	14.3±2.6	0.54
History of Smoking	67.8%	69.7%	58.3%	0.06
Statin Use	57.4%	62.8%	30.6%	<0.001
Hypertension	53.5%	55.3%	44.4%	0.09
Diabetes Mellitus	20.6%	21.4%	16.7%	0.36
PVD	28.6%	29.0%	26.9%	0.73
Symptomatic Status	39.4%	38.6%	43.1%	0.48
Cross Clamp Duration, mins	42.9±17.1	43.0±1.0	42.2±2.1	0.71
NLR	3.4±2.9	2.4±1.0	8.0±4.6	<0.001
Cognitive Dysfunction	24.3%	12.8%	34.7%	<0.001

* Mean ± standard deviation; BMI – body mass index, PVD – peripheral vascular disease, NLR – neutrophil-lymphocyte ratio

† P values of univariate comparisons of the characteristic between patients with NLR <5 and ≥5

Table III

Patient Characteristics by Tertile Categorization*.

	All Patients N=432	Low N=144	Middle N=144	High N=144
Age >75	28.2%	25.0%	27.1%	32.6%
Sex, male	64.1%	63.2%	63.2%	66.0%
BMI, kg/m^2	26.9±4.5	26.9±4.3	27.2±5.0	26.5±4.1
Years of Education	14.5±3.4	14.8±3.3	14.3±3.3	14.6±3.6
History of Smoking	67.8%	70.8%	66.0%	66.7%
Statin Use	57.4%	66.0%	57.4%	48.6%
Hypertension	53.5%	50.7%	58.3%	51.4%
Diabetes Mellitus	20.6%	19.4%	22.9%	19.4%
PVD	28.6%	32.1%	27.0%	26.7%
Symptomatic Status	39.4%	38.2%	42.4%	37.5%
Cross Clamp Duration, mins	42.9±17.1	41.5±16.6	43.3±18.1	43.7±16.6
NLR	3.4±2.9	1.5±0.4	2.6±0.4	6.0±3.8
Cognitive Dysfunction	16.4%	6.9%	17.4%	25.0%

*Mean ± standard deviation; BMI – body mass index, PVD – peripheral vascular disease, NLR – neutrophil-lymphocyte ratio

Table IV

Univariate and Multivariate Logistic Regression Model*.

	Univariate Odds Ratio	P	Multivariate Odds Ratio	P
Age >75 years	1.27 (0.72–2.17)	0.40		
Sex, male	1.48 (0.88–2.48)	0.14	1.16 (0.65–2.05)	0.61
Education, per year	1.09 (1.01–1.18)	0.04	1.07 (0.98–1.17)	0.12
BMI, per kg/m^2	1.00 (0.95–1.06)	0.94		
History of Smoking	1.07 (0.62–1.88)	0.81		
Hypertension	1.07 (0.64–1.80)	0.79		
Statin Use	0.39 (0.23–0.65)	<0.001	0.48 (0.27–0.84)	0.01
Diabetes Mellitus	1.81 (1.00–3.18)	0.05	2.03 (1.08–3.75)	0.03
PVD	1.30 (0.73–2.42)	0.37		
Symptomatic Status	0.81 (0.48–1.36)	0.42		
Cross Clamp Duration, per min	1.01 (0.99–1.03)	0.32		
NLR ≥5	3.63 (2.03–6.43)	<0.001	3.38 (1.81–6.27)	<0.001

*BMI – body mass index, PVD – peripheral vascular disease, NLR- neutrophil-lymphocyte ratio