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Lipid Profiles in Out-of-Hospital Sudden Unexpected Death

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Abstract

Objective: To determine the association between serum lipid measurements and the occurrence of out-of-hospital sudden unexpected death (OHSUD).

Patients and Methods: We compared 139 OHSUD cases (43 female patients [30.9%]) and 968 controls (539 female patients [55.7%]) from Wake County, North Carolina, from March 1, 2013, through February 28, 2015. Individuals were included if they were aged 18 to 64 years and had lipid measurements in the 5 years before their death (cases) or the most recent health care encounter (controls). Covariates were abstracted from medical records for all subjects, and those with triglyceride (TG) levels greater than 400 mg/dL (to convert to mmol/L, multiply by 0.0259) were excluded for low-density lipoprotein (LDL)—related analyses.

Results: By linear regression using age- and sex-adjusted models, cases of OHSUD had lower adjusted mean total cholesterol (170.3±52.2 mg/dL vs 188.9±39.7 mg/dL; $P<.001$), LDL cholesterol (90.9±39.6 mg/dL vs 109.6±35.2 mg/dL; $P<.001$), and non—high-density lipoprotein (HDL) (121.6±49.8 mg/dL vs 134.3±39.6 mg/dL; $P<.001$) levels and a higher adjusted TG/HDL-C ratio (4.7±7 vs 3±2.7; $P<.001$) than did controls. By logistic regression using age- and sex-adjusted models, the odds of OHSUD were elevated per unit increase in TG/HDL-C ratio (1.08; 95% CI, 1.03-1.12).

Conclusion: Out-of-hospital sudden unexpected death cases had more favorable levels of total cholesterol, LDL cholesterol, and non-HDL, possibly indicating a lack of association between traditional lipid cardiovascular risk factors and sudden unexpected death. A comparatively elevated TG/HDL-C ratio in cases may corroborate an evolving hypothesis of how vasoactive and prothrombotic remnant-like lipoprotein particles contribute to sudden unexpected death.

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Sudden death remains a public health challenge, despite substantial progress in identifying associated clinical, structural, and genetic factors,[1,2] with an annual incidence ranging from 150,000 to 400,000 in the United States. Attempts to further elucidate characteristics predictive of sudden death are therefore crucial for identifying populations at risk and instituting preventive measures.

The association between high total cholesterol (TC) levels,[3] high low-density lipoprotein cholesterol (LDL-C) levels,[4] high triglyceride (TG) levels,[5] low high-density lipoprotein cholesterol (HDL-C) levels, and cardiovascular risk is well known. However, few studies have examined the relationship between lipid measurements and sudden death, with varied conclusions. Large prospective cohort studies have found both an elevated[6,7] and a similar[8] risk of sudden death associated with higher baseline TC measurements. Postmortem studies have reported higher levels of remnant lipoprotein particles (RLPs) in cases of sudden death.[9]

There is a lack of comprehensive data on lipid measurements in nonelderly adults temporally closer to death. We aimed to fill this gap by conducting a case-control study comparing lipid profiles of out-of-hospital sudden unexpected death (OHSUD) cases with available lipid profiles with those who did not experience sudden unexpected death within a population-based case-control study from Wake County, a socioeconomically and racially diverse region in North Carolina. We hypothesized that sudden death cases would have a similar or less favorable lipid profile relative to control subjects.

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PATIENTS AND METHODS

The Sudden Unexpected Death in North Carolina (SUDDEN) study is an ongoing population-based registry of adjudicated premature OHSUD cases in North Carolina. The SUDDEN study aims to capture all natural OHSUDs and includes sudden death cases regardless of whether the fatal event was witnessed and/or resuscitation attempted by using criteria similar to those of the Resuscitation Outcomes Consortium for out-of-hospital cardiac arrest.[10] The pilot study was conducted from March 1, 2013, through February 28, 2015, in Wake County, NC, a diverse and predominantly urban region (2015 population estimate: 1,024,198; 21.3% blacks[11]).

Out-of-Hospital Sudden Unexpected Death Cases. Cases of OHSUD were adjudicated according the pilot criteria for the SUDDEN study described elsewhere.[12] We briefly present them here. All emergency medical services (EMS)—attended out-of-hospital deaths occurring from March 1, 2013, through February 28, 2015, in North Carolina residents aged 18 to 64 years were queried from Wake County EMS patient care reporting software. We then excluded those not "free living" such as inmates of prisons/correctional institutions, residents of skilled nursing facilities/hospice, and individuals with "do not resuscitate" orders. Those who had nonnatural/violent deaths were also excluded using information from EMS narratives, medical examiner, and/or autopsy reports (Figure 1). For all included cases, we requested medical records of 5 years preceding death from area health care providers. A committee of cardiologists reviewed all records acquired to adjudicate the sudden and unexpected nature of death for a case. For the present study, we included only adjudicated OHSUD cases with 1 or more lipid panel within their medical records.

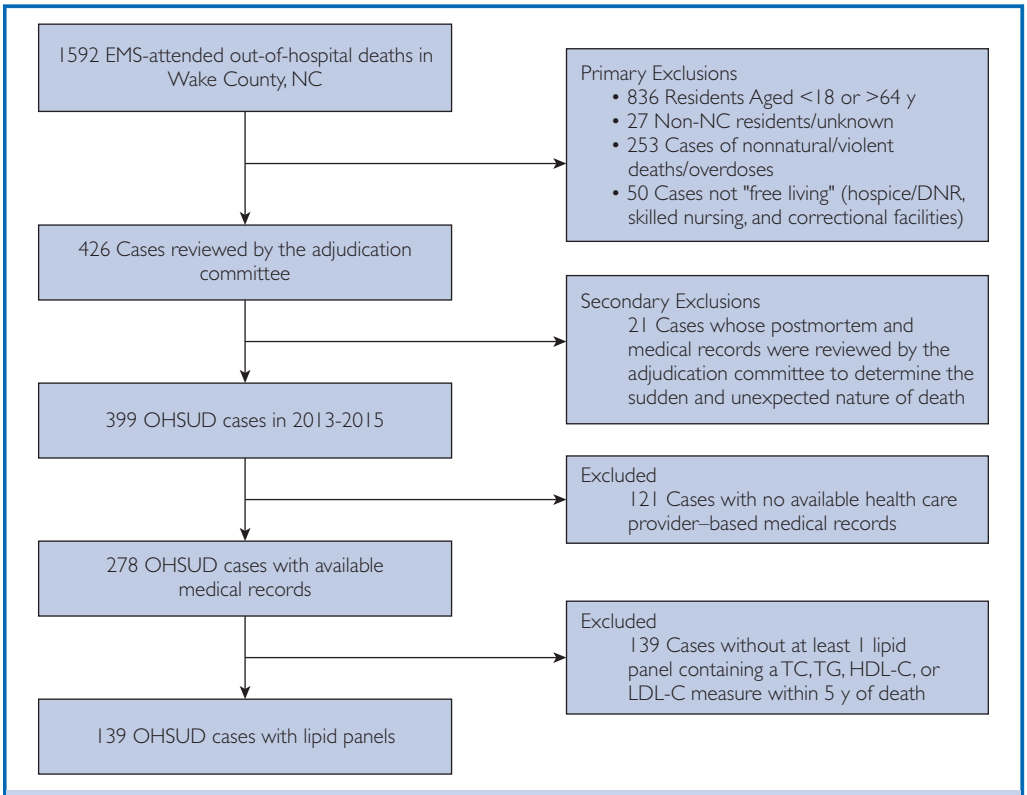

FIGURE 1. Ascertainment of OHSUD cases. DNR = do not resuscitate; EMS = emergency medical services; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; OHSUD = out-of-hospital sudden unexpected death; TC = total cholesterol; TG = triglyceride.

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