突然死患者の死後遺伝子検査は患者の血縁者において費用対効果に優れる

突然死患者の遺伝子を死後に検査し患者の血縁者のリスクを同定することは費用対効果に優れる

Postmortem genetic tests after sudden death may provide less expensive way to identify risk to surviving relatives

原因不明の突然死(SUD)に関連する遺伝子変異を同定する死後標的検査は、第一度近親者に包括的な循環器系検査を施行するよりも経費が少なく有効な方法であるとの研究結果が2009年American Heart Association学会で発表された。研究者らは146のSUD症例において、心臓突然死(SCD)に関連する2つの遺伝性の心調律異常について死後検査の費用を比較した。突然死した患者の26.7%においてQT延長症候群(LQTS)またはカテコールアミン誘発性多形性心室頻拍(CPVT)に関連した疾患を引き起こす可能性のある変異が認められた。その後、突然死した人の中で変異の認められた者の近親者160人における疾患を標的とした評価の経費およびgenotype-negativeの第一度近親者(424人)の全般的な臨床評価の経費を推算した。死亡した人々の遺伝子検査、およびその検査で変異が陽性であった者の近親者160人の疾患を標的とした循環器的評価、および変異陰性の突然死した者の第一度近親者424人の全般的な臨床評価全てにかかる経費は678万ドルと推定された。一方、現在推奨されているSUD患者の近親者584人全員に対する一次循環器的評価の後に疾患を標的とした遺伝子検査を行う方法では700万ドルを超えるであろうと考えられた。

Full Text

Targeted postmortem testing to identify genetic mutations associated with sudden unexplained death (SUD) is an effective and less expensive way to determine risk to relatives than comprehensive cardiac testing of first degree relatives, according to research presented at the American Heart Association's Scientific Sessions 2009.

Postmortem genetic testing can identify mutations that cause cellular dysfunctions leading to heart rhythm disturbances that can cause sudden cardiac death. Such inherited genetic defects occur in 25 to 30 percent of SUD victims, according to lead researcher Michael J. Ackerman, M.D., Ph.D., pediatric cardiologist and director of the Long QT Syndrome Clinic and the Windland Smith Rice Sudden Death Genomics Laboratory at the Mayo Clinic in Rochester, Minn.

Ackerman and senior research technologist David Tester, B.S., compared the yield and costs of postmortem genetic/molecular autopsy testing in 146 SUD cases. They found that 40 of the victims (26.7 percent) had either a catecholaminergic polymorphic ventricular tachycardia (CPVT) mutation (18) or a long QT syndrome mutation (22), both known contributors to sudden death. Researchers estimated the costs of testing 160 relatives of victims who tested positive for mutations. The tests included genetic tests and either treadmill stress tests or electrocardiograms.

For the 424 relatives of the 106 victims who tested negative for mutations, researchers estimated the cost to do more extensive clinical cardiac testing.

Researchers estimated that the total cost of doing postmortem genetic testing, genetic confirmation testing of relatives of mutation-positive victims, followed by cardiac tests for both relatives of mutation-positive and mutation-negative SUD victims, was $6.78 million.

In contrast, the total cost associated with what is currently recommended - comprehensive cardiac testing for all 584 relatives of the SUD victims, regardless of mutation status, followed by directed genetic testing - would have exceeded $7.7 million.
The researchers' primary endpoint, which they reached, was to see if the postmortem testing model would be less expensive and, if so, how great the savings might be.

"With less than 150 SUD cases, use of a cardiac channel molecular autopsy would be estimated to save almost $1 million dollars indicating a much less expensive way of evaluating those left behind," Tester said. "If you identify a mutation in a sudden unexplained death victim, you can do a simple genetic test in first-degree relatives to assess their risk and perform a disorder-directed clinical evaluation rather than a full clinical evaluation. If a relative is negative for the causative mutation, they may not need to undergo further clinical evaluation at all, and that saves money."

The researchers said that insurance companies pay for comprehensive cardiac testing for family members despite the fact that commercial molecular/genetic testing of the deceased can provide just as accurate a risk profile and in many cases minimize the need for clinical testing.

"We are reporting that there is data available to make such cardiac risk evaluations on both sides of the grave," said Ackerman. "The real question is whether it is more prudent and effective to have sudden unexplained death surveillance in autopsy-negative cases. Some insurers cover postmortem gene testing, but it is the exception, not the rule."

The prevalence of the mutations in the SUD autopsies and first-degree relatives was comparable to rates reported by European researchers.

"Clinical screening can be much more selective if there is postmortem gene testing for the defects that result in sodium and potassium channelopathies," said Ackerman. "Currently, however, evaluations of the surviving family members are insurance-covered medical expenses whereas postmortem genetic testing has generally been denied."

The study had limitations and needs to be corroborated by further research. "The cohort we studied was not a population-based collection of SUD cases but instead involved cases that were referred by coroner's/medical examiner's throughout North America so we don't know what the true yield of postmortem genetic testing for autopsy negative SUD is at this time," said Tester.
Coauthors include Argelia Medeiros-Domingo, M.D., Ph.D.; Carla M. Haglund, B.A.; and Jonathan N. Johnson, M.D.

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