ApoB/ApoA1 ratio improves clinical criteria sensitivity for the identification of FH children

Medeiros, AM1; Alves, AC1; Aguiar, P2; Bourbon, M1

on behalf of the investigators of the Portuguese FH Study

1. Unidade de I&D, Grupo de Investigação Cardiovascular, Departamento de Promoção da Saúde e Prevenção de Doenças Não Transmissíveis, Instituto Nacional de Saúde Dr. Ricardo Jorge, Lisboa, Portugal
2. Grupo de Epidemiologia e Estatística, Escola Nacional de Saúde Pública, Universidade Nova de Lisboa, Portugal

Email: mafalda.bourbon@insa.min-saude.pt

1.337 cases

AIM

Familial hypercholesterolemia (FH) is a common autosomal dominant disorder of lipid metabolism. The high levels of plasma cholesterol since birth confers an increased risk of coronary heart disease. Clinical diagnosis of FH is usually done using a set of criteria (MEDPED or Simon Broome Registry (SBR)), however only SBR presents criteria for children. The present work aims to identify useful biomarkers for clinical criteria improvement in clinical settings.

METHODS

A cohort of 237 unrelated children with clinical diagnosis of FH was analysed. Genetic diagnosis of FH was performed by the analysis of LDLR, APOB and PCSK9. ROC curves were performed for lipids and lipoproteins using pre-treatment values of FH and non-FH children to determine novel cut-off values. Different clinical criteria were established using novel cut-off points and compared with genetic diagnosis using cross-tables. Statistical analysis was performed using SPSS v.17 software.

RESULTS

• The cohort was divided according to the genetic diagnosis for further analysis (89 FH children vs 148 non-FH children) (Fig. 1).

• Areas under the curve (AUC) were determined for total cholesterol (0.743), LDL-C (0.743), apoA1 (0.750), apoB (0.820) and apoB/apoA1 ratio (0.835) (Fig. 2).

• Optimal cut-off points were obtained for LDL-C ≥190mg/dL (sensitivity: 72.5%; specificity: 70.3%) and apoB/apoA1 ratio ≥0.68 (sensitivity: 80.0%; specificity: 76.9%) (Table 1).

• SBR criteria revealed a reasonable balance between sensitivity (SS) and specificity (SP) in the identification of index cases (SS: 76.0%; SP: 68.6%) but revealed a low sensitivity in the identification of relatives with FH (SS: 36.0%; SP: 100.0%) (Table 2).

• A combination of SBR criteria with TC≥260mg/dL and/or LDL-C ≥190mg/dL and/or apoB/apoA1 ratio ≥0.68 was found to represent the optimal balance between sensitivity and specificity for the identification of index cases (SS: 86.0%; SP: 68.6%), relatives (SS: 84.0%; SP: 75.0%) and both (SS: 85.0%; SP: 70.8%) (Table 2).

CONCLUSIONS

Our results suggest that determination of apoB/apoA1 ratio could be a useful biomarker to help distinguish FH children from other dyslipidemic children in clinical settings. The inclusion in clinical criteria of a higher cut-off point for LDL-C and an apoB/apoA1 ratio ≥0.68 optimized the criteria sensitivity and specificity. The correct identification and stratification, at an early age, of all children at-risk is of great importance so specific interventions can be implemented.

ApoB/ApoA1 ratio improves clinical criteria sensitivity for the identification of FH children

Medeiros, AM1; Alves, AC1; Aguiar, P2; Bourbon, M1

on behalf of the investigators of the Portuguese FH Study

1. Unidade de I&D, Grupo de Investigação Cardiovascular, Departamento de Promoção da Saúde e Prevenção de Doenças Não Transmissíveis, Instituto Nacional de Saúde Dr. Ricardo Jorge, Lisboa, Portugal
2. Grupo de Epidemiologia e Estatística, Escola Nacional de Saúde Pública, Universidade Nova de Lisboa, Portugal

Email: mafalda.bourbon@insa.min-saude.pt

1.337 cases

AIM

Familial hypercholesterolemia (FH) is a common autosomal dominant disorder of lipid metabolism. The high levels of plasma cholesterol since birth confers an increased risk of coronary heart disease. Clinical diagnosis of FH is usually done using a set of criteria (MEDPED or Simon Broome Registry (SBR)), however only SBR presents criteria for children. The present work aims to identify useful biomarkers for clinical criteria improvement in clinical settings.

METHODS

A cohort of 237 unrelated children with clinical diagnosis of FH was analysed. Genetic diagnosis of FH was performed by the analysis of LDLR, APOB and PCSK9. ROC curves were performed for lipids and lipoproteins using pre-treatment values of FH and non-FH children to determine novel cut-off values. Different clinical criteria were established using novel cut-off points and compared with genetic diagnosis using cross-tables. Statistical analysis was performed using SPSS v.17 software.

RESULTS

• The cohort was divided according to the genetic diagnosis for further analysis (89 FH children vs 148 non-FH children) (Fig. 1).

• Areas under the curve (AUC) were determined for total cholesterol (0.743), LDL-C (0.743), apoA1 (0.750), apoB (0.820) and apoB/apoA1 ratio (0.835) (Fig. 2).

• Optimal cut-off points were obtained for LDL-C ≥190mg/dL (sensitivity: 72.5%; specificity: 70.3%) and apoB/apoA1 ratio ≥0.68 (sensitivity: 80.0%; specificity: 76.9%) (Table 1).

• SBR criteria revealed a reasonable balance between sensitivity (SS) and specificity (SP) in the identification of index cases (SS: 76.0%; SP: 68.6%) but revealed a low sensitivity in the identification of relatives with FH (SS: 36.0%; SP: 100.0%) (Table 2).

• A combination of SBR criteria with TC≥260mg/dL and/or LDL-C ≥190mg/dL and/or apoB/apoA1 ratio ≥0.68 was found to represent the optimal balance between sensitivity and specificity for the identification of index cases (SS: 86.0%; SP: 68.6%), relatives (SS: 84.0%; SP: 75.0%) and both (SS: 85.0%; SP: 70.8%) (Table 2).

CONCLUSIONS

Our results suggest that determination of apoB/apoA1 ratio could be a useful biomarker to help distinguish FH children from other dyslipidemic children in clinical settings. The inclusion in clinical criteria of a higher cut-off point for LDL-C and an apoB/apoA1 ratio ≥0.68 optimized the criteria sensitivity and specificity. The correct identification and stratification, at an early age, of all children at-risk is of great importance so specific interventions can be implemented.

ACKNOWLEDGMENTS

Ana Margarida Medeiros was funded by BRU-OFS/2012; Projects grants: Portuguese Cardiology Society [D13123], Science and Technology Foundation [project grant PIC/C/8333/2007] and Strategic Project Grant [PEst-OE/BIA/UI04046/2011].