た。なお、2011 年の国民健康・栄養調査における LDL-C（F 式）を用いた年齢階級別の平均値（服薬者を除く）と比較してみると、男女とも神戸ではやや平均よりも高く鶴岡は同程度であった。また、non HDL は、鶴岡の男女とも各年代とも同調査報告の平均値（服薬者を除く）よりも低かった。non HDL と LDL-C の差は、神戸研究の集団に比して鶴岡メタボロームコホート研究の集団が男女とも大きい。non HDL には VLDL コレステロールが含まれることから、神戸は健康集団であり肥満者が少なく身体活動量が多いため、VLDL が少ないことにより non HDL と LDL-C の差が一般集団である鶴岡に比して小さい値であったと推測された。

最後に、吹田研究のデータを用いた non HDL の適切なカットオフ値に対する検討からは 185～195 mg/dL 以上（ATP III 基準±25～35mg/dL）が虚血性心疾患発症スクリーニングのためのカットオフ値として適当と考えられた。一方、non HDL と同様の方法で LDL-C の最適カットオフ値を探索したところ 160 もしくは 170 mg/dL 以上（ATP III 基準もしくは+10mg/dL）と考えられた。また、虚血性心疾患に対する non HDL と LDL-C の診断能は比較した場合、ほぼ同等か統計学的な有意差はつかないものの、non HDL の方が優れている事が示された。

前述の横断的検討等は異なり、吹田研究を基にした縦断的検討では non HDL の適切なカットオフ値が従来、LDL-C の管理目標値達成後の二次目標値である LDL-C+30mg/dL 前後と考えられた。しかしながら、本検討結果は単一コホートによる結果であるため、イベント発生数が限られており、より詳細な検討を行う事が困難である。例えば、男女別に解析を行った場合、カットオフ値によってはイベント発生数が一桁台となるため、調整変数として考えている他の危険因子の個数も考慮すると十分なイベント発生数とは言えず、得られた解析結果の信頼性に乏しい。

今後、統合研究などを利用して複数のコホート研究のデータもしくは個人データを統合して、より統計学的なパワーのある研究を行う必要があると考えらえるが、比較・解析に必要な TC・HDL-C・TG を全て空腹条件下で測定している研究が少ない事や、循環器疾患イベントの定義が異なるなど、クリアすべき問題点も多いのが現状である。

一方、臨床検査学的検討により、以下の 4 点が明らかになった。

① non HDL の推定式に必要な TC と HDL-C について、TC についてはすでに、世界的に現在の測定法の正確度は確認されているが、HDL-C 直接法については十分になされていなかったため、この点を確認した。その結果、我が国で用いられている 12 社の試薬を検討したところ 3 社の試薬を除いて、ほぼ正確な測定がなされていることが証明され、non HDL を推定するための条件は担保されたといえる。ただし、3 社の試薬については今後も改良が求められるものと思われる。

② LDL-C の直接法の検討からは、初年度までの検討では、我が国で用いられている 12 試薬について検討したところ、その半数において正確度に問題があることが判明した。この発表により、多くの試薬メーカーにおいて、2 社の試薬では試薬の改良がおこなわれ、2 社の試薬は市場撤退した。比較的良好な 4 試薬について再度検討したところ、健常者ではほぼ正確

度が担保されていることが判明した。今後も問題となっている試薬については、改良もしくは市場撤退を求めていき、すべての試薬の正確度が担保されることを期待するものである。

③ どのような条件下で、LDL-C 直接法を用いることができるかという点についても検討した。少なくとも食前、食後の測定では変化が認められず、食事の影響は除去されたと考えていいと思われる。一方で、III 型や IV 型、V 型など著明な高 TG 血症を認める場合は、外れ値を示すことが多いことから、このような脂質異常症においては、十分な注意が必要とされるものと思われる。また、極端な高 HDL-C 血症や胆汁うっ滞などでも正確な値を示さないことからこのような疾病がある場合は LDL-C 直接法は用いることができないものと考えられた。

④ non HDL については、アポ B との相関を調べているが、やはり、TG の上昇とともにアポ B とのかい離が認められるようになり、TG 600mg/dl 以上では正確度に問題があることは十分認識しておく必要があることが判明した。

以上のことから、non HDL をスクリーニングに用いることは、ほぼ問題ないと考えられるが、TG 600mg/dl 以上の場合には正確度に問題があるが、TG 600mg/dl 以上であれば、受診勧奨の対象になることから特定健診では問題にならないものと思われる。一方、LDL-C 直接法は、試薬の改善により、健常者においてはある程度用いることが可能な状況になっているものと思われる。しかし、III 型のように必ずしも受診勧奨にならないような脂質異常症においても正確度が担保されないということは問題であり、一部の試薬はまだ十分な正確度が担保されていないことは認識しておく必要があるものと思われる。

E．結論

本研究の結果から

1、　non HDLはCAD発症予測のスクリーニング検査としてLDL-Cに勝るとも劣らないマーカーである。

2、　non HDLを185～195 mg/dL以上が、一般住民集団における虚血性心疾患発症スクリーニングのためのカットオフ値として適当と考えらた。

3、　LDL-C直接法については、この間の研究から正確度の劣る試薬は市場から撤退もしくは改善され、ほぼ健常者の場合、食事に関係なく正確度は保証された。

4、　LDL-C直接法はIII型、IV型、V型など著しい高TG血症では正確度が失われ、胆汁うっ滞性肝疾患でも正確度が保証されないなどの問題点に留意する必要がある。

5、　いっぽう、non HDLについてもTGが600mg/dl以上では正確度が欠けることが判明し、この点も留意すべきである。

6、　以上のことから、特定健診においてnon HDLを検査項目として取り入れることは妥当と考えられた。

F．健康危険情報

該当なし

G.研究発表

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H. 知的財産権の出願・登録状況

該当なし。

Ⅱ．研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

【寺本　民生】

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Teramoto T, et al.	Committee Report1 Executive summary of the Japan Atherosclerosis Society(JAS) Guidelines for the Diagnosis and Prevention of Atherosclerotic cardiovascular Diseases in Japan-2012 Version	J Atheroscler Thromb	20(6)	517-523	2013
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