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ORIGINAL ARTICLE

Use of statins and serum levels of Prostate Specific Antigen

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KEYWORDS
Path analysis;
Prostate cancer;
Prostate Specific Antigen (PSA);
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Abstract
Objectives: To quantify the effect of statins' use on Prostate Specific Antigen (PSA) levels in patients referred to prostate biopsy and to determinate if the exposure to statins must be considered to improve the prostate cancer diagnostic accuracy of PSA.
Methods: We selected 551 subjects with PSA <10.0 ng/mL, referred to ultrasound guided transrectal prostate biopsy and classified as cancer or non-cancer patients after biopsy. Information regarding statins' use was obtained from clinical records. We used path analysis to quantify the direct (reflects the influence on PSA biology and metabolism) indirect (reflects the influence on PSA through the effect on the risk of prostate cancer) and total effects (net result of direct and indirect effects) of statins' use on PSA. We used Receiver Operating Characteristic curves to assess the global predictive accuracy of models including PSA, age, body mass index, 5-α-reductase inhibitors, aspirin and statins' use for distinguishing between prostate cancer and benign conditions.
Results: We observed a negative total effect of statins on PSA levels (users vs. non-users: −0.633 ng/mL; 95% CI: −1.087; −0.179), which corresponds to approximately 8.9% lower levels among statins' users, mostly due to the direct effect (−0.588 ng/mL; 95% CI: −1.034, −0.141) rather than that by the indirect effect (−0.045 ng/mL; 95% CI: −0.152, 0.061). There were no statistically significant differences between the area under the curve corresponding to the models with or without statins ($P = 0.274$).

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Conclusion: In patients referred to prostate biopsy, statins' use contributed to lower Prostate Specific Antigen levels, but the clinical impact in these patients is low.

PALAVRAS-CHAVE
Path analysis;
Cancro da próstata;
Antigénio específico da próstata (PSA);
Estatinas

Uso de estatinas e níveis séricos do antigénio específico da próstata

Resumo
Objetivos: Quantificar o efeito do uso de estatinas nos níveis do antigénio específico da próstata (PSA) em doentes submetidos a biópsia prostática. Determinar se o uso de a estatinas deve ser considerado para melhorar a validade do PSA no diagnóstico de cancro.
Métodos: Selecionámos 551 doentes com PSA < 10,0 ng/mL, referidos para biópsia prostática e classificados como «cancro» e «não-cancro» após biópsia. A informação relativa ao uso de estatinas obteve-se nos registos clínicos dos doentes. Usámos «path analysis» para quantificar os efeitos direto (reflete a influência na biologia e metabolismo do PSA), indireto (reflete a influência no PSA através do efeito no risco de cancro da próstata) e total (soma dos efeitos direto e indireto) do uso de estatinas nos valores de PSA. Usámos curvas ROC para avaliar a validade de modelos que incluíam os valores de PSA, idade, índice de massa corporal, uso de inibidores da 5-α-reductase, uso de aspirina e estatinas para distinguir entre cancro da próstata ou situações benignas.
Resultados: Observámos um efeito total negativo das estatinas nos níveis de PSA (utilizadores vs. não-utilizadores: −0,633 ng/mL; 95% CI: −1,087; −0,179), correspondendo, aproximadamente, a níveis 8,9% menores com estatinas, devido principalmente ao seu efeito direto (−0,588 ng/mL; 95% CI: −1,034, −0,141) em vez do efeito indireto (−0,045 ng/mL; 95% CI: −0,152, 0,061). Não houve diferenças estatisticamente significativas entre as áreas sob a curva dos modelos com e sem estatinas (p = 0,274).
Conclusão: Nos doentes referidos para biópsia, o uso de estatinas contribuiu para menores valores de PSA; o impacto clínico nestes doentes é baixo.

Introduction

The use of statins has been increasing over the last two decades[1,2] due to the definition of successively lower cut-offs for cholesterol levels associated with high cardiovascular risk,[3] the changes in the spectrum of statins' indication – with recommendations for its use in both primary and secondary prevention of cardiovascular events –[3] and the intense marketing policies by pharmaceutical companies.[4,5] Currently, statins are among the most prescribed drugs within countries of the Organization for the Economic Co-operation and Development (OECD), with an estimated average daily consumption of 91 Defined Daily Doses (DDDs) per 1000 people.[6]

In addition to the lipid lowering properties of statins, these drugs have shown anti-inflammatory, anti-invasive, tumor growth suppressing, apoptotic and angiogenesis inhibiting properties, potentially decreasing the risk of several cancers,[7] including prostate cancer.[7–9] Statins may also contribute to a reduction in total Prostate Specific Antigen (PSA) levels due to their action on benign prostatic tissue, and on the metabolism of cholesterol – a precursor in the synthesis of PSA.[9] Epidemiological evidence supports a lower risk of prostate cancer among statins users, and several observational studies have shown that non-cancer patients under treatment with statins, especially long therapy courses, present lower levels of serum PSA.[10–12]

The impact of statins on serum PSA levels may lead to a decrease in prostate cancer detection when using the traditional cut-offs for reference to biopsy,[11,13] and adjustment of the PSA threshold may be needed among statins' users, to maximize sensitivity and specificity.[14]

Therefore, we aimed to quantify the effect of using statins on PSA levels, and to assess the potential impact of the exposure to these drugs in the diagnostic accuracy of PSA, among patients referred to prostate biopsy.

Methods

Study population and data sources

Between October 2009 and November 2012, we consecutively recruited patients, at the Department of Urology of Hospital de São João, Porto, Portugal, referred to ultrasound guided trans-rectal prostate biopsy on the basis of abnormal digital rectal examination (DRE) or PSA ≥2.5 ng/mL, and