

Toenail trace elements and risk of Barrett's oesophagus and oesophageal adenocarcinoma: results from the FINBAR study

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Oesophageal adenocarcinoma (OAC) remains a significant and increasing global health problem⁽¹⁾, particularly in Western countries where its incidence has risen significantly. The subject of much conjecture⁽²⁾, given that their levels of exposure are potentially modifiable, many trace elements have been cited as either inhibitory or causative agents of cancer. For instance, selenium (Se), an essential trace element, has been shown to have anti-oxidative, anti-mutagenic, antiviral and anti-carcinogenic properties^(3,4); however, the role of trace elements in OAC has been infrequently investigated.

We examined the association between toenail concentrations of Se and Zn and risk of oesophageal adenocarcinoma and Barrett's oesophagus (BO) amongst 540 participants recruited into the FINBAR (Factors INfluencing the Barrett's Adenocarcinoma Relationship) study that had provided toenail clippings from each hallux. Subjects were recruited between March 2002 and December 2004 and toenail clippings were obtained from 137 OAC cases, 182 BO cases and 221 healthy controls. Toenail trace element concentrations were determined using Instrumental Neutron Activation Analysis. Multiple logistic regression analysis was used to investigate the association between tertiles of toenail trace element concentrations and cancer/BO risk; healthy controls were used as the reference group.

In multivariate analysis, we found no association between toenail Se levels and OAC, RR, highest versus lowest tertile, 0.91 (95% CI 0.43, 1.93; $P = 0.81$), or BO, RR 0.96 (95% CI 0.44, 2.1; $P = 0.93$). Higher toenail Zn status was associated with a two-fold increased risk of BO, RR, highest v. lowest tertile, 2.25 (95% CI 1.05–4.86; $P = 0.04$); there was no association between toenail Zn levels and risk of OAC.

To our knowledge, this is the first case-control study investigating toenail trace element levels and risk of OAC or BO. Despite the known antioxidant capacity of Se, we observed no evidence of a reduced risk for these conditions. Interestingly our analysis showed a doubling of risk of BO among subjects with the highest toenail zinc concentrations; reasons for this association are largely unknown, but may be related to tissue Zn deposition, as tissues that accumulate Zn also concentrate Cd – a known carcinogen. A recent prospective study, the first to segregate analysis by histological subtypes in a Western population⁽⁵⁾, has provided evidence of an inverse association between toenail Se levels and oesophageal squamous cell carcinoma and gastric cardia cancer; no clear association was observed between the toenail selenium levels and OAC. Associations appeared strongest for those with a low intake of antioxidants, strengthening the hypothesis of an antioxidant mechanism; in general however, the means and stage of carcinogenesis by which trace elements may exert their effects remains poorly understood.

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