

Smoking

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GUIDELINES

No recommendations possible based on Level I or II evidence.

SUGGESTION FOR CLINICAL CARE

(Suggestions are based on Level III and IV sources)

- **Smoking is associated with more severe proteinuria and renal failure progression in patients with kidney disease. (Level II–III evidence; numerous large retrospective cohort studies; clinically relevant outcomes; consistent strong effects) The clinical evidence for this association is stronger for diabetic patients than for non-diabetic patients.**
- **Cessation of smoking has been associated with retardation of renal failure progression. (Level II–III evidence; several small cohort studies; clinically relevant outcomes; consistent strong effects)**

Background

Smoking has been associated with accelerated renal failure progression. The objective of this guideline is to evaluate the available clinical evidence pertaining to the impact of smoking on renal function decline in chronic kidney disease (CKD).

Search Strategy:

Databases searched: Medline (1996 to November Week 2, 2003). MeSH terms for kidney disease were combined with MeSH terms for smoking. The results were then limited to cohort and case-control studies.

Date of search: 16 December 2003.

What is the evidence?

There are no randomised controlled trials (RCTs).

The evidence for a deleterious effect of smoking is stronger for diabetics than non-diabetics, but is limited to retrospective analysis. In addition to the recall bias and case selection bias inherent in such studies, the association of smoking with the

development of renal failure does not establish whether smoking promotes kidney disease or whether smoking is merely associated with other factors that promote kidney disease (such as non-compliance, vascular disease, hypertension, etc.).

A retrospective, case-control study using data obtained from 4142 non-diabetic, elderly (> 65 yrs) participants of the Cardiovascular Health Study Cohort identified that current smoking was a significant, independent risk factor for clinically important changes in renal function (increase in serum creatinine of at least 0.3 mg/dL, odds ratio 2.1, 95% CI: 1.3–3.6). Former smokers were not at increased risk, suggesting that cessation of smoking is associated with a reduction in risk of progressive kidney disease.

Stengel et al (2003) retrospectively analysed data from a non-concurrent cohort study of 9082 US adults, aged 30–74 years, who participated in the second National Health and Nutrition Examination Survey (NHANES II) from 1976 to 1980. Up until 1992, 189 incident cases of either treated end-stage kidney disease (ESKD) or CKD-related death were identified. The study observed that, compared with never-smokers, the adjusted relative risk of CKD was significantly increased in smokers of more than 20 cigarettes a day (RR 2.3, 95% CI: 1.3–4.2), but not in smokers of 1–20 cigarettes per day (RR 1.2, 95% CI: 0.7–2.3).

In a prospective study of 51 patients with severe essential hypertension followed for a mean period of 35.5 months, smoking was identified by multivariate regression analysis as the most powerful, independent predictor of decreases in both the reciprocal creatinine slope over time and the calculated GFR (Regalado et al 2000).

A retrospective cohort study of 160 adults with lupus nephritis (Ward and Studenski 1992) followed for a median of 6.4 years demonstrated in a Cox's proportional hazard analysis, that smoking at the onset of nephritis was associated with a hazard ratio of 2.05 (95% CI: 1.07–3.93) for ESKD.

In a retrospective cohort study of patients with polycystic kidney disease, Chapman et al (1994) observed that individuals with significant proteinuria had a greater number of cigarette pack years than those without proteinuria.

Smoking is a significant independent predictor of significant renal artery stenosis in elderly patients beginning renal replacement therapy (Appel et al 1995).

In retrospective studies of diabetic patients, smoking has been associated with an increased risk of microalbuminuria (Muhlhauser et al 1986, Couper et al 1994, Almdal et al 1994, Chase et al 1991, Rossing et al 2002, Gambaro et al 2001), a shortened time interval between onset of diabetes and onset of albuminuria (Stegmayr et al 1987), an accelerated rate of progression from microalbuminuria to persistent proteinuria (Muhlhauser et al 1986, Rossing et al 2002, Gambaro et al 2001) and an accelerated progression of diabetic nephropathy to ESKD (Stegmayr and Lithner 1987). Improved blood pressure control and angiotensin-converting enzyme inhibition do not appear to abrogate the risk associated with smoking in diabetic nephropathy (Chuahirun et al 2002, Chuahirun et al 2003). However, there is some conflicting data in that a prospective observational cohort study of 301 albuminuric Type 1 diabetics followed for at least 3 years at the Steno Diabetes Centre was unable to demonstrate statistically significant differences in GFR decline between non-smokers, former smokers or current smokers (Hovind et al 2003). These negative results may reflect a type 2 statistical

error.

Smoking cessation has been associated with a reduction in albumin excretion (Chase et al 1991) and renal failure progression in diabetics (Sawicki et al 1994). In 45 patients with progressive non-diabetic nephropathy (chronic glomerulonephritis or tubulointerstitial nephritis) who were encouraged to stop smoking (1–2 packs per day), 16 successfully stopped smoking and demonstrated a significantly slower rate of decline in creatinine clearance over 2 years compared with the 26 patients who continued to smoke (Schiffel et al 2002). Compliance was assessed by carboxyhaemoglobin measurements performed every 6 months.

Summary of the evidence

There are no RCTs. Numerous retrospective and prospective studies (some of which have included thousands of patients) have suggested that smoking is associated with renal failure progression in both diabetic and non-diabetic kidney disease. Current smoking confers a greater risk than former smoking. Three small cohort studies suggest that cessation of smoking may ameliorate kidney failure progression in diabetic and non-diabetic CKD.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative: No recommendation.

UK Renal Association: No recommendation.

Canadian Society of Nephrology: No recommendation.

European Best Practice Guidelines: No recommendation.

International Guidelines: No recommendation.

Implementation and audit

No recommendation.

Suggestions for future research

No recommendation.

References

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Out of date

Appendices

Out of date