Smoking and kidney

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The prevalence of cigarette smoking in 2015 was 16.7% among adult males and 13.6% among adult females . Prevalence was highest among adults aged 25–44 years (14.8%) and lowest among persons aged ≥65 years

everyday 3800 youth under the age of 18 start smoking . Most adult smokers, 88%, smoked their first cigarette before the age of 18

Cigarettes are designed to allow deep inhalation of smoke into the lungs, delivering high levels of nicotine to the brain within 10–20 s of inhalation

Electronic cigarettes, on the other hand, are rapidly increasing in use: approximately 28% of high school students and 11% of middle school students are current electronic cigarette users.

(WHO) reports that among adults over 15 years, the global rate of smoking declined from 23.5% in 2007 to 20.7 in 2015, reflecting a 2.8% smoking rate reduction

the number of people smoking worldwide has remained at 1.1 billion from 2007 to 2015 because of population growth

Smoking tobacco increases the risks for a wide range of chronic conditions, including cancer,
cardiovascular diseases
(coronary heart disease, stroke, and heart failure), respiratory diseases,
and chronic kidney disease (CKD).

Population-based studies have identified cigarette smoking as an independent risk factor for various manifestations of CKD, including proteinuria, elevated serum creatinine levels, decreased eGFR, and development of ESKD or death associated with CKD

Nicotine acts as a ganglionic nicotinic cholinergic agonist in the autonomic ganglia, brain, spinal cord, neuromuscular junctions and adrenal medulla . Nicotine has dose-dependent pharmacological effects and has both stimulant and depressant action

The effects of nicotine on the central nervous system (CNS) and its peripheral stimulating effects are mediated through the release of several neurotransmitters, including acetylcholine, beta-endorphin, dopamine, norepinephrine, serotonin, and adrenocorticotropic hormone (ACTH)

Notable stimulant effects of nicotine stimulant activities include peripheral vasoconstriction, elevated blood pressure, tachycardia, increased cardiac output, and enhanced mental alertness and cognitive function

Depressant effects of nicotine include muscle relaxation and anxiety reduction

Nicotine is well distributed with a volume of distribution of about 2.6 L/kg . It undergoes primarily hepatic (80–90%) metabolism—with the remainder of the metabolism taking place in the lungs and kidney—to inactive metabolite: cotinine. Nicotine has a half-life of 1–4 h and about 2–35% is excreted unchanged in the urine

Cancer

Smoking is currently the largest preventable cause of cancer-related deaths, accounting for approximately 30% of cancer related deaths

A causal relationship has been established between cigarette (tobacco) smoking and lung cancer, the leading cause of cancer-related deaths in the U.S. There is also a causal relationship between cigarette smoking and cancers of the head, neck, liver, bladder, cervix, esophagus, colon, and rectum

Cardiovascular Diseases

Major mechanisms underlying smoking-induced cardiovascular disease include endothelial dysfunction, prothrombotic effects, inflammation, altered lipid metabolism, increased demand for myocardial oxygen and blood, decreased supply of myocardial blood and oxygen, and insulin resistance

Respiratory Diseases

smoking is the primary cause of COPD in the U.S

may exacerbate asthma in adults.

increases the risk of developing tuberculosis and dying from tuberculosis

Additional Effects

impairs immune function, resulting in an increased risk of pulmonary infections and rheumatoid arthritis

increasing the risk of peptic ulcer disease.

smokers with diabetes have a higher risk of developing complications, including nephropathy, blindness, peripheral neuropathy, and amputations

Cigarette smoke damages a wide range of immunological functions, including innate and adaptive immune responses

Emerging literature demonstrates that inflammasome constitutes an essential component in innate immune response.

smoking plays an important role in promoting worsening of proteinuria and progression of diabetic nephropathy, particularly in type I diabetes (TIDM)

effects of NIC on glomerular renal disease are at least in part mediated by direct injurious effects of NIC on glomerular podocytes, including increased generation of reactive oxygen species (ROS), apoptosis, and reduced synaptopodin (SYNPO), a major molecule involved in the stabilization of the glomerular basement membrane.

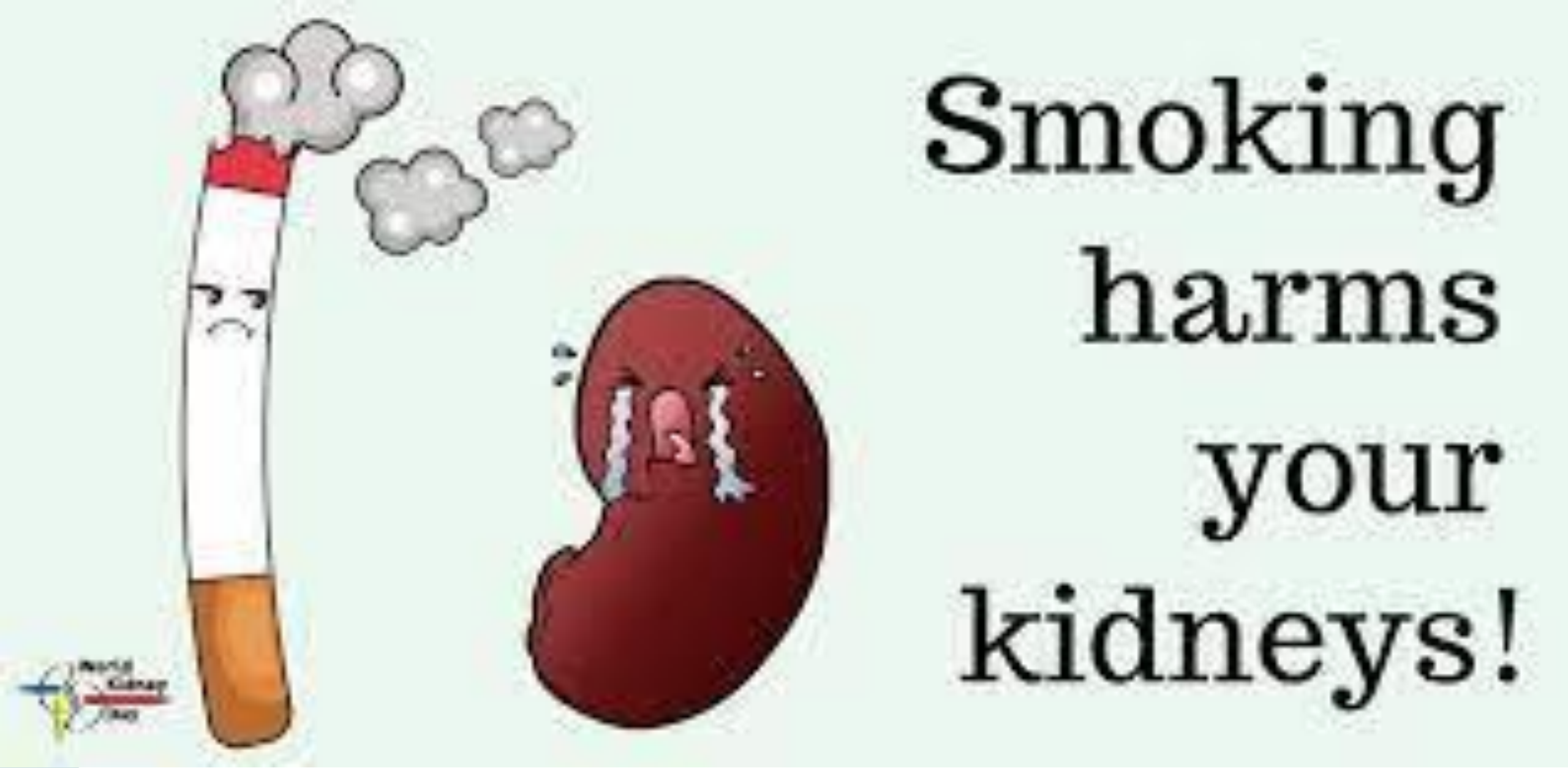
NIC Potentiates oxLDL-Induced Podocyte Apoptosis Through a CD36-Dependent Mechanism

NIC upregulates the expression of CD36 in human THP1-differentiated macrophages

CD36 is involved in the regulation of lipid metabolism associated with oxLDL in podocytes and that NIC enhances CD36-mediated lipid accumulation in human podocytes through upregulation of CD36.

the administration of NIC to wild-type mice had no significant effect on fibronectin expression but resulted in a significant increase in fibronectin in diabetic mice.

while foci of cortical scarring were observed in 50% of diabetic mice on tap water, 100% of diabetic mice on NIC had evidence of cortical scarring.


Smoking
harms
your
kidneys!

Potential Mechanisms of Smoking-Induced Renal Damage

Possible mechanisms whereby cigarette smoking may con tribute to renal damage include sympathetic nervous system activation

glomerular capillary hypertension,

Endothelial cell injury, and direct tubulotoxocity.

Smoking

↓

Sympathoadrenal activation

↓

Increase in circulating catecholamines

↓

β1-adrenergic stimulation

↓

Increase in renin production

↓

Angiotensin II

Most of the effects of tobacco exposure are dose and time dependent and could be ameliorated with smoking cessation.

nicotine has powerful mitogenic effects and induces extracellular matrix production in human mesangial cells via reactive oxygen species generation. These effects of nicotine may play a major role in the pathogenic mechanisms that mediate the deleterious effects of smoking in renal disease.

CIGARETTE SMOKING AND BLOOD PRESSURE

Acute effects

are related to sympathetic nervous system overactivity, which leads to an increase in blood pressure, heart rate, myocardial contractility, and myocardial oxygen consumption

The rise in blood pressure with each cigarette is transient, and this transient increase may be most prominent with the first cigarette of the day, even in those who smoke cigarettes habitually.

the average elevation in systolic pressure after the first cigarette of the day was approximately 20 mmHg

Blood pressure began to fall 10 to 15 minutes after smoking ceased, and no pressor effect was detected after 30 minutes.

Chronic effects of cigarette smoking

There are inconsistent data that cigarette smoking raises blood pressure chronically or increases the incidence of hypertension.

In many, but not all studies, individuals who smoke cigarettes habitually had lower blood pressure than nonsmokers

This finding might be related to the following:

- Those who smoke cigarettes generally have a lower body weight compared with those who do not smoke

Cotinine, the major metabolite of nicotine, has a vasodilator effect that might also contribute to lower blood pressure in those who smoke

However, cigarette smoking increases the risk of masked hypertension

Cigarette smoking increases arterial stiffness, which may persist for a decade after smoking cessation

Cigarette smoking increases the risk of renovascular hypertension

Several studies documented that smoking is an independent predictor of (micro)albuminuria in otherwise healthy hypertensive subjects. The prevalence of microalbuminuria is almost double in smoking than nonsmoking lean patients with primary hypertension (12).

A recent study (15) found that patient nsion and left ventricular hypertrophy smoking >20 cigarettes/d had a 1.6-fold higher prevalence of microalbuminuria and a 3.7-fold higher prevalence of macroalbuminuria than never-smokers

Cigarette smoking is associated with severe hypertensive retinopathy (often called "malignant hypertension") ; whether or not this relation is the result of renovascular hypertension is unknown.

Although smoking may not increase the risk of new-onset hypertension, it markedly increases the risk of atherosclerotic cardiovascular events and end-stage kidney disease in patients with hypertension

The mechanism underlying the adverse effect on kidney function is unclear but may be related to smoking-induced, transient increases in systemic blood pressure that are then transmitted to the glomerulus, resulting in glomerular hypertension

e-cigarettes are associated with a mild, short-term increase in diastolic pressure and a mild, short-term increase or no effect on systolic blood pressure

In a retrospective, case-control study of 89 cigarette smokers with hypertension, switching from combustible tobacco cigarettes to e-cigarettes was associated with a reduction in systolic and diastolic blood pressure at 12 months (-10 mmHg and -6 mmHg, respectively)

HOOKAH (WATER PIPE) SMOKING AND BLOOD PRESSURE

indirect and direct evidence suggest that hookah smoking has blood pressure and other cardiovascular effects similar to cigarette smoking.

hookah smoking for 15 to 30 minutes acutely increased systolic pressure (by 3 to 16 mmHg) and diastolic pressure (by 2 to 14 mmHg)

Adverse Renal Effects of Smoking in Patients with Renal Disease

Diabetic Nephropathy

The first reports that documented an increased renal risk in smokers were retrospective studies in patients with type 1 diabetes. In 1978, Christiansen (18) provided evidence that smokers have a higher risk to develop diabetic nephropathy than nonsmokers.

Diabetic nephropathy was present in 13% of patients who smoked <10 cigarettes/d but in >25% in patients who smoked 30 cigarettes/d. Subsequently, numerous studies confirmed the increased renal risk in smokers with type 1 and type 2 diabetes mellitus

The a[redacted]e literature documents that smoking (1) increases the risk to develop microalbuminuria (14,20-30), (2) accelerates the rate of progression from microalbuminuria to manifest proteinuria (31-36), and (3) accelerates progression of renal failure (32,37-40).

Chase *et al.* (20) reported that in a group of 359 young subjects with type 1 diabetes the prevalence of borderline (>7.6 μg/min) and frankly e n) urinary albumin excretion rate was 2.8-fold higher in smokers than nonsmokers.

the impact of smoking on the rate of progression is similar in t
2 diabetes. The rate of decline in GFR is approximately 55% higher in smokers compared with nonsmokers.

Hypertension, hyperglycemia, dyslipidemia, and cigarette smoking (CS) are major risk factors that contribute to the progression of diabetic nephropathy (DN).

stable reactive aldehydes in CS induce endothelial injury via mechanisms that involve activation of NADPH oxidase and increased oxidative stress

Nondiabetic Renal Disease

PRIMARY RENAL DISEASE

at entry was related to the decline in GFR after 3.2 yr of follow-up: in patients with chronic glomerulonephritis, the loss of GFR was 5.3 ml/min per yr in heavy smokers but only 2.5 ml/min per yr in nonsmokers. Thus, smoking appears to double the rate of progression in patients with chronic glomerulonephritis

SYSTEMIC DISEASES INVOLVING THE KIDNEY

A retrospective cohort study on 160 patients with a median follow-up of 6.4 yr documented [redacted] the time of onset of lupus nephritis was an independent risk factor for more rapid progression to ESRD(55).

The hypothesis tha the nent and/or progression of pauci-immune ANCA-positive lonephritis has been forwarded (57) but without supporting data.

smoking-induced endothelial cell damage may predispose to the formation of antibodies against nuclear cell antigens extruded from endothelial cells or endothelial cell adherent polynuclear cells.

in passing that in patients with anti-glomerular basement membrane glomerulonephritis smoking strikingly increases the risk of pulmonary hemorrhage (Goodpasture syndrome) (1)

a combination of arteriolar and atheroembolic damage (*i.e.*, cholesterol microembolism) is thought to contribute to progressive loss of renal functio y, smoking is a known risk factor for cholesterol microembolism (64)

Smoking and Atherosclerotic Renal Artery Stenosis/Ischemic Nephropathy

The prevalence of renal vascular stenosis is higher in patients with peripheral vascular disease (59). The latter is common in smokers; it is not therefore surprising that smokers have a higher risk of critical atherosclerotic renal artery stenosis (60,61).

a high proportion of patients with unilateral (62) or bilateral (63) atherosclerotic renal artery stenosis are smokers

Pathohistologic Features of Smoking-Induced Renal Damage

In a renal biopsy study, the histologic findings of 107 patients with chronic renal failure were assessed to investigate the effect of smoking on glomerulosclerosis and vascular damage (72)

Smoking was not associated with the severity of glomerulosclerosis.

Compared with nonsmokers, ever-smokers exhibited more severe myointimal hyperplasia. This finding was particularly evident in patients >50 yr of age.

our group found more severe glomerulosclerosis and tubulointerstitial fibrosis in the subtotally nephrectomized rat treated with a cigarette smoke extract dissolved in acetone (74)

glomerular basement width in patients with type 2 diabetes who smoke has been reported in a preliminary biopsy study (75).

Excess risk of renal allograft loss associated with cigarette smoking

Pretransplant smoking was significantly associated with reduced overall graft and death-censored graft survival.

Patients who were smokers at the time of pretransplant evaluation had kidney graft survival of 84%, 65%, and 48% at 1, 5, and 10 years, respectively, compared with graft survival in nonsmokers of 88%, 78%, and 62% (P=0.007).

In a multivariate analysis, pretransplant smoking was associated with a relative risk of 2.3 for graft loss

Among patients with a smoking history before transplantation, death-censored graft survival was significantly higher for those who quit smoking before transplant evaluation.

Cigarette smoking is associated with higher eGFR compared to non-smoking. This difference was more pronounced in males than females

The higher prevalence of proteinuria in smokers suggests a mechanism of hyperfiltration, which might result in future progressive renal damage

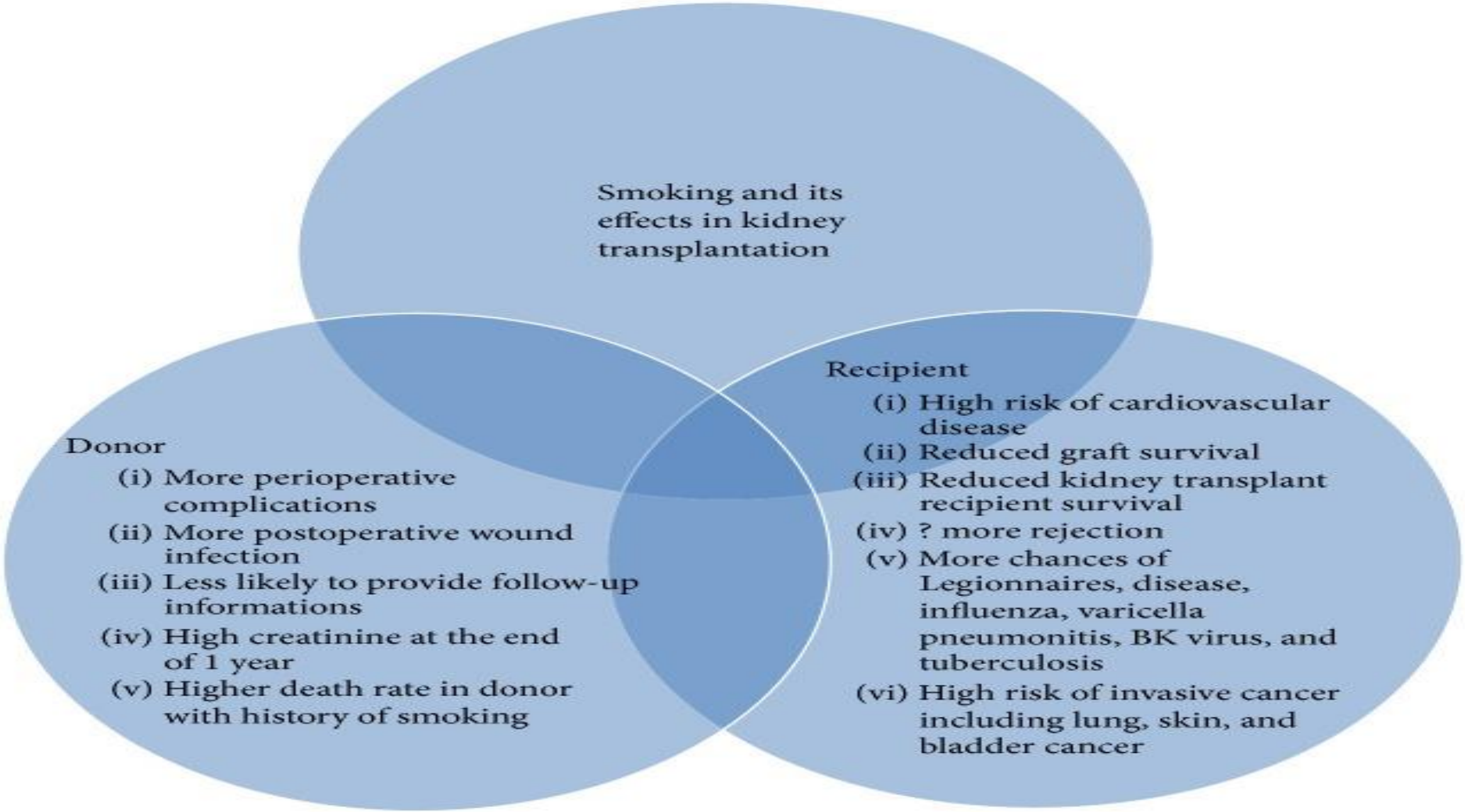
Cigarette smoking in living kidney donors: donor and recipient outcomes

Donor smoking at time of evaluation did not significantly decrease allograft survival (HR = 1.19, p = 0.52), but recipient smoking at evaluation did reduce allograft survival (HR = 1.74, p = 0.05).

Both donor and recipient smoking decreased recipient survival (HR = 1.93, $p < 0.01$ vs HR = 1.74, $p = 0.048$).

Cigarette Smoking and Its Hazards in Kidney Transplantation

Kidney donors with history of cigarette smoking are prone to develop perioperative complications, pneumonia, and wound infection.


Smoking and its effects in kidney transplantation
Donor
(i) More perioperative complications
(ii) More postoperative wound infection
(iii) Less likely to provide follow-up informations
(iv) High creatinine at the end of 1 year
(v) Higher death rate in donor with history of smoking
Recipient
(i) High risk of cardiovascular disease
(ii) Reduced graft survival
(iii) Reduced kidney transplant recipient survival
(iv) ? more rejection
(v) More chances of Legionnaires, disease, influenza, varicella pneumonitis, BK virus, and tuberculosis
(vi) High risk of invasive cancer including lung, skin, and bladder cancer

Cigarette smoking may accelerate the progression of IgA nephropathy

cigarette smoking (hazard ratio (HR) = 1.58; p = 0.043) was an independent risk factor predicting poor renal progression in IgAN, and that IgAN patients with chronic kidney disease (CKD) stage 3-4 were more susceptible to cigarette smoking (p < 0.001)

A case–control study revealed that smoking contributed to the progression to chronic renal failure, especially regarding nephrosclerosis and glomerulonephritis

We divided the patients into non-smoker and smoker (current or former) groups. Smoker was defined as having actively smoked > 400 cigarettes in a patient's lifetime

The correlation analyses indicated that smoking was correlated with tubular atrophy/interstitial fibrosis lesions (odds ratio (OR) = 1.826; 95% CI: 1.296–2.573; $p = 0.001$) but not with other pathological lesions.

smoking dose was negatively correlated with eGFR ($r = 0.141$; $p < 0.001$) and positively correlated with proteinuria ($r = 0.096$; $p = 0.001$).

analysis showed that cigarette smoking remained an independent risk factor for IgAN progression

Smokers with > 20 pack-years tended to have higher proportions of tubular atrophy/interstitial fibrosis.

Further analysis showed that patients with more severe renal dysfunction were more susceptible to the effects of cigarette smoking

Further analysis indicated that smokers with hypertension and renal vasculopathy had the worst renal outcomes (before or after PSM), indicating that cigarette smoking, hypertension, and renal vasculopathy could accelerate IgAN progression

Smoking could induce oxidative stress and increase the stiffness of central vessels, causing tubular damage and increasing the risk of tubular atrophy and fibrosis

IgAN patients with stage 3 or 4 CKD should undergo smoking cessation therapy to slow deterioration of the renal disease.

smoking
cessation was associated with less
progression to macroalbu-
minuria and a slower rate of GFR
decline than continued
smoking in patients with diabetes

smoking was associated
with increased all-cause mortality as
well as the combined
endpoint of all-cause mortality and
CKD progression, though not with CKD progression alone

Prevalence of Cigarette Smoking among Patients with Different Histologic Types of Kidney Cancer

Cigarette smoking is causally linked to renal cell carcinoma (RCC).

By histology, proportions of current or formers smokers ranged from 38% in patients with chromophobe carcinoma to 61.9% in those with collecting duct/medullary carcinoma.

Compared with other RCC histologic types, chromophobe RCC has a weaker (if any) association with smoking.

it is rational to conclude that tion is one of the single most effective measures to retard progression of renal failure—quite apart from its undoubtedly beneficial effect on cardiovascular risk (67,85).

Cite

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