Smoking and Transplantation

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Disclosures

None

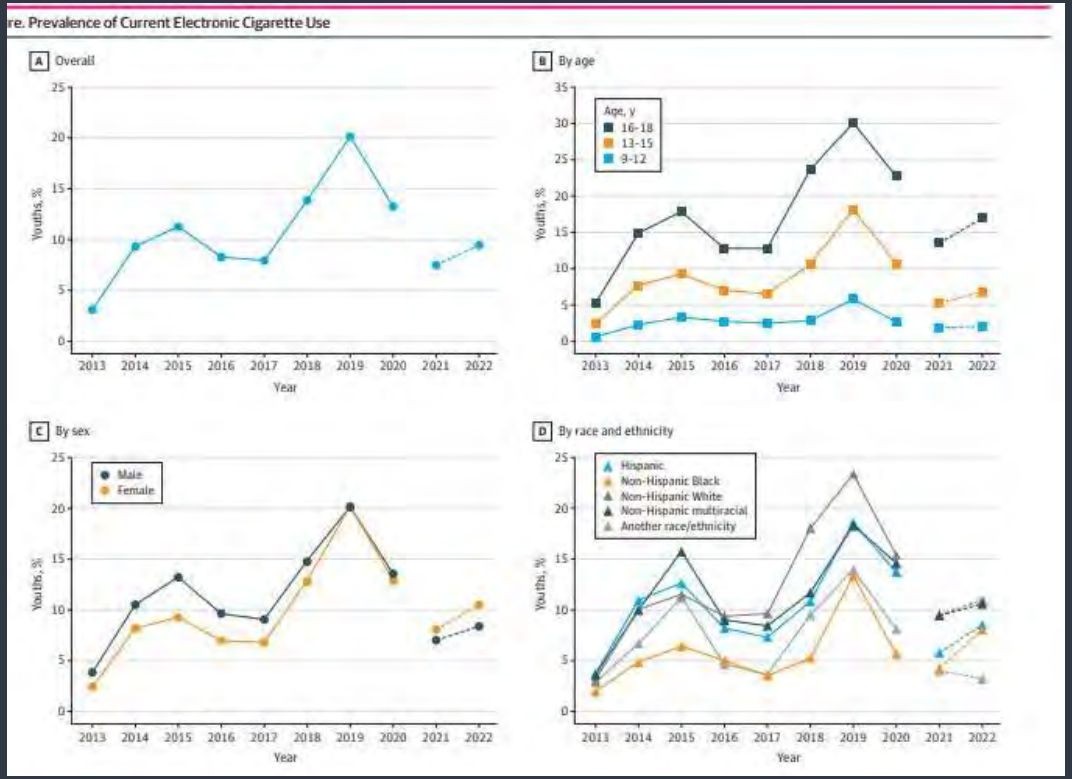
Objectives

1. Provide insight into the prevalence and risks of marijuana and tobacco use in transplant candidates and recipients
2. Ethical concerns of transplanting candidates who smoke
3. discussion on the future of transplantation of candidates who are actively smoking
4. What are centers doing around the US?
5. Case studies and discussion

According to the CDC:

1. 2022: 49.2 million (19.8%) adults with current tobacco use (E-cigs, cigs, smokeless)

2. 52.5 million marijuana users in US (19% of Americans)



Mattingly et al JAMA Network 2024

Tobacco risks to the general population:

Cancer:

- Smokeless tobacco common cancers: mouth, esophageal and pancreatic

- In 2021, nearly 2 of every 25 adults (7.9%) reported using 2 or more tobacco products

CDC.gov

Ischemic Heart Disease

- 8.9 million deaths in 2019- 16% of death worldwide(1)
  - Most common cause of death worldwide
    - For all races and socioeconomic classes
  - 30% of all death annually in the US (>age 35)
- Strongly correlated with smoking and hypertension(1)
  - Men > Women for cigarette smoking
  - Higher smoking rates in the elderly which can accelerate IHD in relation to higher risk associated comorbidities
- Mortality rates for IHD are decreasing with increases in primary prevention and improved diagnostics(1)

Tobacco smoking after transplant:

- Studies show that a substantial number of transplant patients continue to resume smoking post transplant between 11-40%(1)
- Pre transplant substance use including smoking was strongly correlated with post transplant substance use(1)
- Cigarette smoke is a well-known risk factor for morbidity and mortality of transplanted organ function (2)

1. Increased infection risk
2. Increased risk of graft failure/ischemic heart disease
3. Increased risk of cancer, primarily lung
4. Lung injury
5. Delayed wound healing

Cannabis risks to the general population:

System	Cannabis use[a]
Neuropsychiatric	• Impaired cognition, learning, short-term memory, and judgment
	• Impaired motor coordination resulting in increased risk of MVA
	• Depressive disorders
	• Anxiety including social anxiety disorder
	• Psychiatric disturbance (development of schizophrenia, development of bipolar disorder, increased symptoms of mania and hypomania in patients with bipolar disorder, other psychoses)
	• Cannabis use disorder
	• Diminished life satisfaction, achievement, and education outcomes
	• Suicidal ideation, suicide attempts, suicide completion
	• Overdose injuries (including respiratory distress)
	• Withdrawal syndrome (irritability, sleeping difficulty, dysphoria, craving, anxiety)
	• Altered brain development (with initiation in early adolescence)
Pulmonary	• Possible increased infection risk (*Aspergillus* sp, tuberculosis)
	• Respiratory symptoms (cough, increased sputum production, wheeze)
	• Inflammation of large airways, increased airway resistance, lung hyperinflation
	• More frequent episodes of chronic bronchitis
Cardiovascular	• Myocardial infarction trigger
	• Ischemic stroke, TIA
	• SAH
	• Arrhythmia, tachycardia
	• Cardiomyopathy, heart failure, sudden circulatory death
Gastrointestinal	• Cannabinoid hyperemesis syndrome
Musculoskeletal	• None reported
Endocrine /Metabolic	• None reported
Renal	• Acute kidney injury (synthetic cannabinoid use)
	• Membranous glomerulonephritis
	• Hyponatremia
Hepatic	• None reported
Ocular	• None reported
Hematologic/Immune	• Possible increased infection risk (*Aspergillus* sp., tuberculosis)
	• Testicular germ cell tumors

[a]Many effects observed among heavy and long-term cannabis use; causality difficult to establish given confounding factors.
MVA, motor vehicle accident; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack

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THC risks after transplant:

Similar to the risks prior to transplant, but additionally:

Medication interactions

- Immunosuppressants - Increased risk of CNI toxicity
- ‘azoles, diltiazem and warfarin

Vaping THC:

- Additives causing increased numbers of lung injury

CBD (hemp)

- no psychoactive properties
- Anti-inflammatory and anti-proliferative effects
- Potential benefits for anxiety, depression
- Low misuse rate
- Unclear regulations – composition often different from location to location

MDPI.com/journal/life 2021, 11, 1063

Cannabis use and outcomes after SOT:

With a **history** of cannabis use (prior to transplant):

- No difference in death or graft failure at 1 year between users and nonusers
- Cannabis did not effect creatinine
- No 5 year survival difference found between current/former cannabis users in 316 liver txp recipients

Use after transplant:

- Retrospective studies showed that abuse/dependence in the first year post transplant was associated with a significant increase in graft failure, all cause graft loss, and death over 2 years.

Transplantjournal.com. February 2021, volume 105, number 2

The ethical concerns/debate:

Opioids vs Marijuana

- Okay when prescribed by a MD?
- Similar effects, addiction rates, etc

Marijuana vs tobacco

- Light smokers vs heavy smokers
- Attempted to quit in the past?
- Assessments for substance use disorders

Organ Stewardship

- Studies show that a substantial number of transplant patients continue to resume smoking post transplant between 11-40%(1)
- Pre transplant substance use including smoking was strongly correlated with post transplant substance use(1)
- Cigarette smoke is a well-known risk factor for morbidity and mortality of transplanted organ function (2)

Future considerations

1. Transplanting a smoking donor to a smoking recipient
2. Marijuana legalization approaches
3. What else do we need to take into consideration for occasional smokers listing eligibility? drug/nicotine level cut off?

What are centers doing around the US? Internationally?

A 2014 study found that many transplant centers transplant current smokers (Table), with nearly all centers transplanting former smokers.

While desirable to require potential transplant patients to quit smoking, it can also be beneficial to have access to the transplant list sooner to reduce cost, morbidity, and mortality.

While smoking cessation is desirable, withholding access to a life saving transplant as a strict policy does not meet the accepted standard of care.

Transplant Centers	Liver N = 41	Kidney N = 63	Pancreas N = 42	Living Liver Donors N = 20	Living Kidney Donors N = 62
# of Transplants Performed	≤ 40 = 12 41-99 = 24 ≥ 100 = 5	≤ 50 = 23 51-100 = 18 101-150 = 11 > 150 = 11	≤ 8 = 22 8-15 = 13 ≥ 16 = 7	≤ 3 = 9 4-8 = 5 ≥ 9 = 6	≤ 30 = 38 31-60 = 14 ≥ 61 = 10
Transplants Current Smokers	25/51 (61%)	38/63 (60.3%)	14/42 (33.3%)	7/20 (35%)	27/62 (43.5%)
Serum Cotinine Testing Performed	15/41 (36.6%)	19/63 (30.6%)	13/41 (30.9%)	n/a	n/a

ISHLT 2024 Guidelines

Recommendations for Psychosocial Evaluation: Evaluation of Substance Use		
COR	LOE	RECOMMENDATIONS
1	C-EO	1. In heart transplant candidates with a history of active illicit drug use, at least 6 months of abstinence is recommended prior to transplant listing.
2a	B-NR	2. In heart transplant candidates with a history of active cannabis use, recommendation for abstinence prior to evaluation and listing is reasonable due to reported infectious risk and potential drug-drug interaction post-transplant.
1	B-NR	3. In heart transplant candidates with a history of active alcohol use disorder, at least 6 months of abstinence is recommended prior to transplant listing.
1	B-NR	4. In heart transplant candidates with a history of active tobacco smoking, at least 6 months of abstinence is recommended prior to transplant listing.

UNMC Heart Transplant Guidelines

Contraindications for Heart Transplantation

Age > 75 and/or limited life expectancy.

Systemic diseases

severe peripheral vascular or cerebrovascular disease

poorly controlled diabetes

Hgb A1c > 10

multiple complications

chronic pulmonary disease

Active systemic infection (VAD line infections are excluded).

Irreversible pulmonary hypertension (PAP >60mmHg) with TPG >15 and PVR >5 not responding to vasodilator challenge.

Acute PE (within 6 months).

Severe parenchymatous lung disease with FEV1 < 40% and DLCO < 40%.

Active malignancy or within last 5 years (needs oncology evaluation before consideration with statement of 10-year prognosis).

Severe pre-renal azotemia and/or hepatic abnormalities (they may be accepted if mild to moderate in severity and secondary to heart failure).

Patients may be considered for multi-organ (heart-kidney, heart-liver) transplant in selected situations; if GFR < 40 ml/min, bilirubin > 2.5 mf/dL or transaminases > 2x normal.

Obesity (BMI > 35 or weight greater than 150% of predicted ideal body weight). Carefully selected patients with BMI up to 40 may be considered.

History of unresolved alcohol, tobacco, drug abuse, or significant psychiatric illness. Should be documented free of alcohol or drug abuse and free of smoking (including nicotine from vaping) for ≥ 6 months. (Exception: nicotine replacement therapies prescribed by the provider).

Case presentation

47 year old male with past history of NICM (dx age 32), CRT-D, VT s/p impella assisted VT ablation. Pt with positive family history of heart failure, medical marijuana use and history of tobacco use. He was doing well with medical management until June of last year when he was hospitalized with VT storm associated with hypokalemia.

He smokes an oil form of marijuana approximately every other week to manage chronic right shoulder and neck pain. His pain began approximately 2 years ago after a treadmill injury during a cardiopulmonary exercise test. States that he prefers to use marijuana for pain control rather than narcotics. He admits to marijuana use prior to his shoulder injury. He states he will be cigarette free in 2 months, but continues to use nicotine in the form of pouches to curb his cigarette cravings. He is using one 3 mg pouch daily of nicotine. Denies current alcohol use.

He was previously employed as a butcher but was instructed to refrain from working due to his heart disease following his most recent hospitalization.

Discussion...

Our decision:

Pt discussed at PSC. Discussion with team regarding pt medical marijuana card and history of smoking cigarettes and occasional cigars (pt reports has stopped). Committee decision that at this time would like pt to continue to prove negative nicotine screens. Under current guidelines would need pt to stop all marijuana use to be considered for advanced therapies. Pt is agreeable to STOP all medical marijuana use. He states he usually only used it maybe 1 time per week for his chronic shoulder pain as he didn't like using narcotics. He is agreeable to monthly drugs of abuse and urine nicotine screens.

Received DT LVAD at OSH roughly 3 weeks later - scheduled procedure, non-urgently

Case #2:

This is a 51 y.o. male suffered a cardiac arrest while at home. EMS called, and on arrival to OSH, he was found to have STEMI and was taken for coronary angiogram, found to have severe 3-Vessel coronary disease including 90% LM lesion. Attempts were made to intervene with the lesions but he became increasingly unstable and was taken emergently to the OR for revascularization. He suffered a cardiac arrest with both PEA and VT, CPR was performed for 30mins and patient was subsequently placed on VA ECMO.

SW assessment (obtained from pt's wife)

Alcohol/drug/tobacco Use:

What is average alcohol use per week or month:

2-3 glasses of red wine 3-4 evenings per week.

Do you feel your alcohol usage has impacted your lifestyle?

No, denies any problematic drinking or legal charges related to his use.

Do you use tobacco?

yes, she knows he has smoked for at least 15 years (before they were together). She is unsure of the amount because he is not allowed to smoke in the house or car. She recently found chantix gum so believes he was trying to quit. He has quit for a few months before in the past.

Psychology Assessment (done with wife):
DSM-5 DIAGNOSTIC IMPRESSIONS:

1. Tobacco use disorder
2. R/O Adjustment disorder with anxiety

On admission

METABOLIC STUDIES	
Homocysteine, Bl	
Nicotine, Ur	67
Cotinine, Ur	177
3-OH-Cotinine, Ur	508
Nornicotine, Ur	16
Anabasine, Ur	<3

Decision:
Denied for transplant, too sick. Recommend LVAD as DT

HM3 LVAD placed as well as centrimag RVAD
Unable to wean RVAD (lactate inrease with wean attempts, continued need for dobutamine support)

Discussion...

Our decision:

Decision made to list patient status 1 for non dischargeable surgically implanted biventricular support.

pt received OHT roughly 2 weeks later.

Post transplant:

1. Compliant, has not returned to smoking (that we are aware of)
2. 6 years post transplant, LHC report below:

Post Operative Diagnosis:

- Right dominant system.
- Small vessel, obstructive CAD involving ostial D1 (70-80% stenosis)
- Diffuse pruning of major coronary arteries, suggestive of mild CAV.
- Episode of complete heart block with no escape rhythm for 15-20 seconds during LV pullback in the beginning of procedure.
- LVEDP 1 mmHg.

3. LHC from 2 years prior:

Description of Findings:
Right dominant system
LM: Bifurcates into LAD and LCx arteries. No angiographic CAD/CAV.
LAD: No angiographic CAD/CAV.
LCX: No angiographic CAD/CAV.
RCA: No angiographic CAD/CAV.

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