The Association Between Hormone Replacement Therapy and The Incidence of Esophageal Cancer in Post-Menopausal Women: A Systematic Review and Meta-Analysis.

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INTRODUCTION

- The incidence of esophageal cancer (EC) has risen in recent decades and tends to be more common in men than women. Yet, the reasons behind this pattern remain unclear. It has been hypothesized that female sex hormones, mainly estrogen, are protective against EC.
- Previous studies have shown that the use of hormone replacement therapy (HRT) reduces the risk of colorectal cancer, but it is associated with an increased risk of gastroesophageal reflux disease, breast, endometrial and ovarian cancers.
- **AIM:** To investigate the association between HRT and the risk of esophageal adenocarcinoma (AC) and squamous cell carcinoma (SCC) in post-menopausal women.

METHODS

- **Databases:** Embase, PubMed/MEDLINE, and Google Scholar
- **Eligible studies:** Retrospective cohort and case-control studies including post-menopausal women who either received HRT or not
- **Primary endpoint:** Association between HRT use and various types of EC
- **Software used:** Review Manager 5.4 software

RESULTS

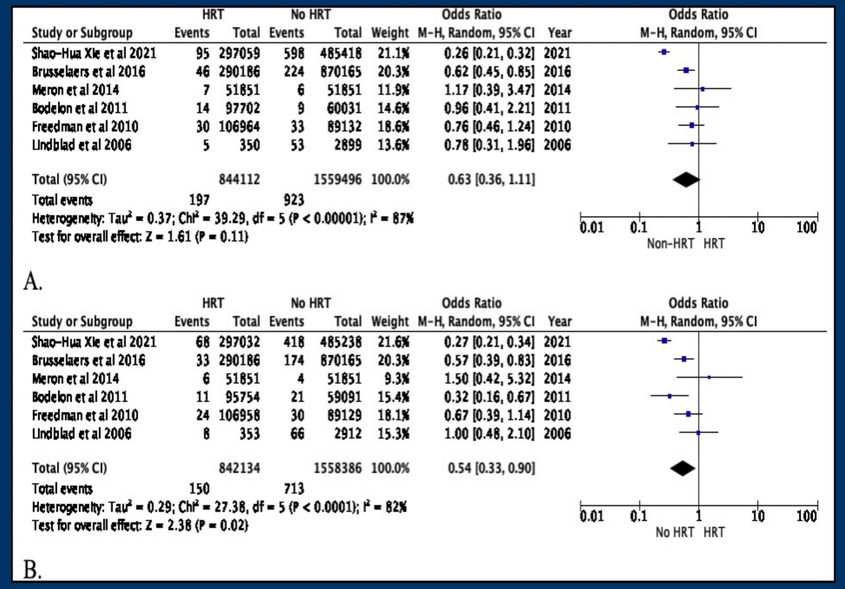

FIGURE 1: Forest plots showing the association between hormone replacement therapy use and the incidence of esophageal adenocarcinoma (A) or squamous cell carcinoma (B).

A.

Outcome	Subgroup	OR [95% CI]	P-value	Test for Subgroup Differences P (I^2 %)
AC	Estrogen only	0.59 [0.29, 1.21]	0.15	0.83 (00.0)
	Estrogen + Progesterone	0.54 [0.32, 0.90]	0.02	
SCC	Estrogen only	0.52 [0.31, 0.89]	0.02	0.03 (78.9)
	Estrogen + Progesterone	0.27 [0.20, 0.36]	<0.00001	

B.

Variables		Rate of Esophageal Cancer (/1000)	OR [95% CI]	P-value
Duration of HRT Use	<10 years	0.142	0.65 [0.35, 1.23]	0.19
	≥ 10 years	0.270		
Status of HRT Use	Past Users	0.212	1.18 [0.57, 2.44]	0.66
	Current Users	0.193		
Menarche Onset	Early (< 12 years)	0.529	1.46 [0.84, 2.53]	0.18
	Late (≥ 15 years)	0.235		
Menopause Onset	Early (<45 years)	0.243	0.99 [0.23, 4.17]	0.99
	Late (≥ 55 years)	0.319		
Age at First Birth	Early (<20 years)	0.511	1.08 [0.52, 2.23]	0.84
	Late (≥ 30 years)	0.273		

TABLE 1: (A) Subgroup analysis investigating the association between different types of hormone replacement therapy (HRT) and the risk of either subtype of esophageal cancer (B) Evaluation of influencing factors affecting the association between HRT use and the risk of esophageal cancer

- 6 studies involving 2,403,608 post-menopausal women who either received HRT or not were included in the pooled analysis
- No statistically significant association between HRT use and esophageal AC (OR=0.63, P=0.11) with similar risk in estrogen only or estrogen + progesterone HRT
- Significantly reduced risk of esophageal SCC in patients receiving HRT (OR=0.54, P=0.02) that is more pronounced with combined estrogen + progesterone therapy compared to estrogen only HRT
- The duration (> or < 10 years), status of HRT use (past or current users), age of menarche, menopause, and first birth were not confounding variables affecting the association

CONCLUSION

- The use of hormone replacement therapy in post-menopausal women was associated with a decreased risk of esophageal squamous cell carcinoma but not adenocarcinoma. In addition, combined estrogen and progesterone therapy was associated with a greater reduction in the risk of esophageal SCC compared to estrogen only therapy.