

Largest-ever analysis of its kind finds Cushing's syndrome triples risk of death

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Endogenous Cushing's syndrome, a rare hormonal disorder, is associated with a threefold increase in death, primarily due to cardiovascular disease and infection, according to a study whose results will be presented at ENDO 2021, the Endocrine Society's annual meeting.

The research, according to the study authors, is the largest systematic review and meta-analysis to date of studies of endogenous (meaning "inside your body") Cushing's <u>syndrome</u>. Whereas Cushing's syndrome most often results from external factors—taking cortisol-like medications such as prednisone—the endogenous type occurs when the body overproduces the hormone cortisol, affecting multiple bodily systems.

Accurate data on the mortality and specific causes of death in people with endogenous Cushing's syndrome are lacking, said the study's lead author, Padiporn Limumpornpetch, M.D., an endocrinologist from Prince of Songkla University, Thailand and Ph.D. student at the University of Leeds in Leeds, U.K. The study analyzed death data from more than 19,000 patients in 92 studies published through January 2021.

"Our results found that <u>death rates</u> have fallen since 2000 but are still unacceptably high," Limumpornpetch said.

Cushing's syndrome affects many parts of the body because cortisol responds to stress, maintains <u>blood pressure</u> and cardiovascular function, regulates blood sugar and keeps the immune system in check. The most



common cause of endogenous Cushing's syndrome is a tumor of the pituitary gland called Cushing's <u>disease</u>, but another cause is a usually benign tumor of the adrenal glands called adrenal Cushing's syndrome. All patients in this study had noncancerous tumors, according to Limumpornpetch.

Overall, the proportion of death from all study cohorts was 5 percent, the researchers reported. The standardized mortality ratio—the ratio of observed deaths in the study group to expected deaths in the general population matched by age and sex—was 3:1, indicating a threefold increase in deaths, she stated.

This mortality ratio was reportedly higher in patients with adrenal Cushing's syndrome versus Cushing's disease and in patients who had active disease versus those in remission. The standardized mortality ratio also was worse in patients with Cushing's disease with larger tumors versus very small tumors (macroadenomas versus microadenomas).

On the positive side, mortality rates were lower after 2000 versus before then, which Limumpornpetch attributed to advances in diagnosis, operative techniques and medico-surgical care.

More than half of observed deaths were due to heart disease (24.7 percent), infections (14.4 percent), cerebrovascular diseases such as stroke or aneurysm (9.4 percent) or blood clots in a vein, known as thromboembolism (4.2 percent).

"The causes of <u>death</u> highlight the need for aggressive management of cardiovascular risk, prevention of thromboembolism and good infection control and emphasize the need to achieve disease remission, normalizing cortisol levels," she said.

Surgery is the mainstay of initial treatment of Cushing's syndrome. If an



operation to remove the tumor fails to put the disease in remission, other treatments are available, such as medications.

Study co-author Victoria Nyaga, Ph.D., of the Belgian Cancer Centre in Brussels, Belgium, developed the Metapreg statistical analysis program used in this study.

Provided by The Endocrine Society

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