

## Adrenal

### ADRENAL – CLINICAL RESEARCH STUDIES

#### *Adrenal Hyperplasia as Possible Predictor of Mortality in Patients Admitted for Suspected SARS-CoV-2 Infection: A Prospective Study*

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A large percentage of patients affected by SARS-CoV-2 disease (COVID) have associated comorbidities such as arterial hypertension, obesity, diabetes mellitus and thrombophilia. On the contrary, the prevalence in COVID patients of diseases of the adrenal glands has not been reported. Since the visualization of the adrenal glands is almost always available in chest CT performed in patients with suspected or confirmed SARS-CoV-2 infection, the evaluation of the frequency and characteristics of morphological disorders of the adrenal masses in such patients appears of interest. We carried out a prospective consecutive series of 402 patients (M 222, 55.2%; F 180, 44.8%) with a median age of 76 years (IQR 64–84 years), admitted in the emergency department for suspected SARS-CoV-2 infection. One hundred patients had a PCR-confirmed diagnosis of infection on a naso-pharyngeal swab (24.9%). All patients underwent a chest MDCT study including the adrenal region and clinical assessment of co-morbidities. Compared to subjects without confirmed disease, COVID patients had more frequently close contact with other positive subjects (24% vs 4.6%,  $p < 0.001$ ), typical symptoms (68% vs 28.5%,  $p < 0.001$ ), and suggestive chest CT findings (90% vs 31.1%,  $p < 0.001$ ). We found altered adrenal morphology in 100 patients (24.9%): 62 subjects had adrenal hyperplasia, which was unilateral in 42 of them (67.7%) and bilateral in 20 (32.3%), while 38 patients had discrete adrenal nodules, unilateral in 34 of them (89.4%) and bilateral in 4 (10.6%). The median size of adrenal nodules was 16 mm (10–50 mm) with a median density of 10 HU (-41 - 42 HU). In 17 patients with adrenal hyperplasia, a previous CT was available for comparison: in all cases an increase in thickness was evident at admission (from 1 to 15 mm, with a median of 1.95 mm increase). COVID patients had a higher frequency of adrenal nodules (12% vs 8.6%,  $p = NS$ ). Sixty-three patients (16%) died. They were older (80 vs 74 years,  $p = 0.001$ ), had a higher frequency of adrenal hyperplasia (25% vs 14%,  $p = 0.03$ ), more frequent active cancer disease (37% vs 19%,  $p = 0.003$ ) and COVID (23% vs 13.2%,  $p = 0.02$ ). In a multivariate model, adrenal hyperplasia is an independent risk factor for mortality (OR 2.52, 1.15–5.55,  $p = 0.02$ ), as well as age (OR 1.04, 1.01–1.07,  $p = 0.005$ ), active oncological disease (OR 3.06, 1.44–6.49,  $p = 0.004$ ), and COVID (OR 2.88, 1.38–6.01,  $p = 0.005$ ). This is the first study reporting the prevalence of morphological alterations of adrenal glands in suspected COVID patients. The frequency of discrete adrenal nodules (9.5%) is in line with the high prevalence of adrenal incidentalomas in

elder subjects. The high frequency of adrenal hyperplasia associated with increased risk of mortality suggests that this may be the consequence of an exaggerated activation of the HPA axis due to a highly stressful condition.

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#### *Adrenocortical Carcinoma Treatment in the Netherlands: An Analysis From the Netherlands Cancer Registry From 2014 to 2019*

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**Background:** Adrenocortical carcinoma (ACC) is a rare disease with often poor prognosis. Previous research has shown that surgery in a Dutch Adrenal Network (DAN) center increases the chance of survival. We aim to explore the determinants and survival of patients with ACC recently treated in the Netherlands both within and outside DAN centers. **Methods:** We analyzed retrospectively collected data from 172 adult patients with newly diagnosed ACC and 97 patients with recurrence or new metastases, registered between 2014 and 2019 in the Netherlands Cancer Registry. Differences in survival were analyzed with cox-regression analysis. **Results:** More than half of the new cases presented with advanced disease (25.7% stage III, 34.6% stage IV) and the median survival was 29 months. The majority of treatments occurred within a DAN center (87.2% of surgery, compared to 56.4% between 1999 and 2009; and 94.5% of medical treatment). There were no differences in patient characteristics between the centers apart from a relatively high number of patients with stage IV disease outside DAN centers (47.2% vs. 28.7%). Adrenal resection and mitotane therapy both resulted in a significant survival benefit (resection HR 0.29, CI95%[0.17–0.49]; mitotane HR 0.61, CI95%[0.37–0.99], corrected for stage). Still, a remarkable proportion of patients with advanced disease received no mitotane treatment (39.8%). Due to the small number of patients treated outside DAN centers, survival benefits could not be tested. **Conclusions:** Centralization of ACC care in the Netherlands has improved since the previous report, but a further improvement in centralization of surgery can be made. Adrenal resection and mitotane treatment remain the main form of treatment, with a clear survival benefit. Further research is necessary to determine why mitotane treatment is withheld in a large proportion of patients with advanced disease.

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#### *Aldosterone-Producing Adenoma: Does a Larger Tumor Secrete More Apparent Cortisol?*

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