



Blood pressure changes with gender-affirming hormone therapy in transgender people

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Since the Sustainable Development Goals were adopted by the United Nations in 2015 and became well known, the recognition of transgender and gender-diverse populations has increased. Gender-affirming hormone therapy (GAHT) is anticipated to be prescribed to more transgender people. However, little has been demonstrated on the association between GAHT and blood pressure (BP).

Martinez-Martin et al. compared the BP change and hypertension incidence risk among young transgender individuals stratified by GAHT status [1]. Their study revealed that the choice of androgen blocker contributed to BP changes in young transgender women. Consequently, the group treated with cyproterone acetate experienced a higher BP elevation than the other groups. The amplitude of the BP increase after 5 years of treatment was 14 mmHg, resulting in 4.90% of patients experiencing new-onset hypertension. Thus, BP elevation may occur as a side effect of the use of cyproterone acetate. Since their study was a nonrandomized retrospective observational study, we should consider the possibility of an indication bias. However, their report contributed an important piece of evidence regarding GAHT among young people. A previous small randomised trial using ambulatory BP monitoring revealed that ethinyl-estradiol plus cyproterone acetate could elevate daytime BP [2]. Another report indicated that cyproterone acetate did not elevate BP [3].

A recent study in the United States revealed that systolic BP decreased by 4 mmHg within 2–4 months of starting GAHT in the transfeminine group, in which several participants were treated with spironolactone (mean dosage, 72.8 mg/day) [4]. This decrease in BP remained for 4.7 months. The result is reasonable because spironolactone has also antihypertensive effect. In the report by Martinez-Martin et al., no significant BP change with spironolactone (median dosage, 125 mg/day) administration was observed [1]. Therefore, BP may have increased more steeply in the population selected by Martinez-Martin et al. than in the other populations. However, based on the results comparing the effect of cyproterone acetate on BP with that of spironolactone, GAHT with spironolactone appears to be safer in regard to adverse BP elevation.

Whether the choice of antiandrogen contributes to an increase in cardiovascular risk remains unclear. A higher cardiovascular risk among transgender women than among cis-gender women is well reported [5, 6]. The use of ethinyl estradiol in transgender women was associated with an elevated risk of cardiovascular death in a study from the Netherlands with a median follow-up of 18.6 years [7]. In this population, ethinyl estradiol appeared to be mostly used with cyproterone acetate [7]. However, in the United States study, in which spironolactone was mainly used as an antiandrogen, it was reported that transgender women were more likely to have a history of myocardial infarction than cis-gender women [6]. A summary of the association between GAHT and cardiovascular risk is presented in Fig. 1.

Cyproterone acetate may suppress testosterone levels more strongly than spironolactone [8]. However, given reports of an increased risk of meningiomas or the association with depression with cyproterone acetate use, transgender women in the United Kingdom are prescribed gonadotropin-releasing hormone agonists [9]. Cyproterone acetate is not used in the United States either [9]. In Japan,

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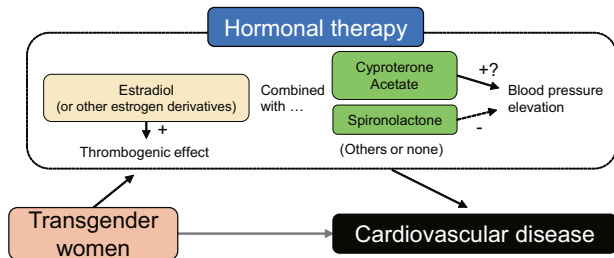


Fig. 1 Summary of the association between GAHT and cardiovascular risk

cyproterone had been approved for treating prostate cancer, but it was discontinued owing to concerns regarding its adverse effects, such as a potentially increased risk of hepatotoxicity.

In the transgender population, BP can change drastically after GAHT. Transgender people can undergo GAHT since they are young. Despite drastic BP elevation such as the 14 mmHg systolic BP elevation reported in the study by Martinez-Martin et al., BP in young people may not reach the hypertension threshold. Therefore, the increased BP in the young transgender population can be overlooked. We should consider that elevated BP increases the lifetime risk of cardiovascular disease, especially in young people [10]. Monitoring changes in BP using methods such as home BP measurement is important after GAHT initiation.

Compliance with ethical standards

Conflict of interest MS received academic contributions from Bayer Yakuin.

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