COMMITTEE REPORT

New definition and classification of “Hypertensive Disorders of Pregnancy (HDP)”

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Why have the definition and classification of pregnancy-induced hypertension been modified?

Key points

- The classification of pregnancy-induced hypertension (PIH) was revised in 2018. In Japan, chronic hypertension had already been excluded from the PIH category before the revision of this classification, based on the view that the clinical conditions of chronic hypertension in pregnancy are different from those of PIH. However, in Europe and North America, chronic hypertension in pregnancy is included in PIH and classified as a whole into the category of hypertensive disorders of pregnancy (HDP), because pregnant patients with chronic hypertension require antihypertensive drugs and are likely to develop preeclampsia.
- The revised classification of PIH in Japan is consistent

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with the international classification of PIH (the classification of hypertensive disorders of pregnancy by the International Society for the Study of Hypertension in Pregnancy [ISSHP]). Namely, PIH including chronic hypertension is generically classified as HDP; hypertension in pregnancy without proteinuria is regarded as preeclampsia when there is organ damage affecting the maternal body or the uteroplacental system; and the definition of early onset is altered from less than 32 weeks of gestation to less than 34 weeks of gestation according to the criteria used in Europe and North America. In addition, the category of mild preeclampsia has been eliminated in recognition of the fact that any case of preeclampsia is not mild. The revised classification according to the worldwide standard will allow us to make a global comparison of the number of patients, the incidence, and the treatment outcomes of HDP.

Brief overview of modifications in the definition and classification of HDP

Key points

- Hypertensive disorders of pregnancy have been newly classified into four disease types, i.e., (1) preeclampsia, (2) gestational hypertension, (3) superimposed preeclampsia, and (4) chronic hypertension, excluding eclampsia in the previous classification of disease types.
- A diagnosis of preeclampsia is made when hypertension is present with maternal organ damage or uteroplacental insufficiency even if there is no proteinuria.
- Classification of the severity of conditions in terms of the amount of urinary protein excretion has been abolished. A severe case is defined as one in which there is severe hypertension, maternal organ damage, and/or uteroplacental insufficiency.
- As for disease type classification, the definition of early onset has been altered from less than 32 weeks of gestation to less than 34 weeks of gestation.

Current status of the internationally recognized ISSHP classification and the definition and classification in various countries other than Japan

Key points

- The ISSHP classification and major overseas classifications include chronic hypertension, whereas chronic hypertension was not included in the previous classification used in Japan.
- International and overseas classifications use the term “hypertensive disorders of pregnancy” including chronic hypertension, whereas the previous Japanese classification used the term “pregnancy induced hypertension” under the definition of newly occurring hypertension at or after 20 weeks of gestation.
- There have been differences in the definition of preeclampsia and the classification of severe cases between Japan and other countries.

Concept of superimposed preeclampsia

Key points

- In Japan, superimposed preeclampsia is defined as “a condition in which renal disease not accompanied by hypertension is present before pregnancy or before 20 weeks of gestation, and hypertension occurs at or after 20 weeks of gestation”, thus including the presence of renal disease not accompanied by hypertension.
- The definition of superimposed preeclampsia used in countries other than Japan does not include the presence of renal disease not accompanied by hypertension, and focuses on pregnant women with hypertension,

showing a slight difference from the definition used in Japan.

- A case in which hypertension is present before pregnancy or before 20 weeks of gestation, and there is accompanying uteroplacental insufficiency at or after 20 weeks of gestation is included in the category of superimposed preeclampsia in Japan, whereas it is not included in this category in the ISSHP classification.

Rationale for the diagnosis of preeclampsia not accompanied by proteinuria

Key points

- As for the diagnosis of preeclampsia not accompanied by proteinuria, a patient is diagnosed as having preeclampsia when hypertension is combined with maternal organ damage and/or uteroplacental insufficiency in accordance with the ISSHP classification even if there is no proteinuria.
- The term preeclampsia in Japanese has not been altered in the recent revision of HDP, and remains as a subject for future consideration.

Handling of uteroplacental insufficiency

Key points

- There is controversy outside of Japan as to whether a diagnosis of preeclampsia should be made when uteroplacental insufficiency without proteinuria is combined with hypertension newly occurring at or after 20 weeks of gestation.
- The ISSHP diagnostic criteria include such cases of preeclampsia based on the view that uteroplacental insufficiency should be included because preeclampsia is etiologically attributed to disturbed placentation in an early stage of pregnancy.
- The new classification in Japan includes cases with uteroplacental insufficiency in the category of preeclampsia, which is consistent with the ISSHP classification.

Definition of “severe” cases

Key points

- In the subclassification of HDP, the diagnosis of a severe case is made when the blood pressure (BP) is within the range of severe hypertension (systolic BP ≥ 160 mmHg or diastolic BP ≥ 110 mmHg), or when there is maternal organ damage (acute renal impairment, liver dysfunction, neurologic complications such as eclampsia, hematologic complications such as thrombocytopenia) and/or uteroplacental insufficiency (e.g., fetal growth restriction) in preeclampsia or superimposed preeclampsia.

The reason for “mild” cases not being included in the definition

Key points

- The term “mild”, as applied to affected cases, has been deleted from the current revised definition. It is necessary for every healthcare provider to recognize that there are no “mild” cases, which can be managed non-aggressively, among HDP cases.
- Hypertensive disorders of pregnancy are considered to be progressive clinical conditions.
- Deletion of the term “mild”, as applied to affected cases, is consistent with various overseas criteria.

Alterations of diagnostic criteria for early onset (EO) and late onset (LO) types

Key points

- The current revision includes the new definition “early onset (EO) is onset occurring within less than 34 weeks of gestation, and late onset (LO) is onset occurring at or after 34 weeks of gestation”.
- The previous classification used the definition “a case occurring within less than 32 weeks of gestation is EO type, and a case occurring at or after 32 weeks of gestation is LO type”.
- The current revision is based on the view that EO and LO types should also be distinguished in terms of 34 weeks of gestation in Japan according to international standards, based on discussions in international academic meetings and articles published in international journals.
- In consideration of the history of the criteria for these conditions, the following additional statement has been made: “There is the opinion in Japan that EO and LO should be distinguished in terms of 32 weeks of gestation, and the cut-off point will be reviewed by the Japan Society for the Study of Hypertension in Pregnancy in the future.
- Investigation of the evaluation of the optimal cut-off value of gestational weeks for EO type preeclampsia has been started, and the results of this investigation will be reflected in the next revision of the definition and classification of HDP.

Organ damage reported in HDP

Key points

- Organ damage in HDP includes gradually progressing maternal liver and kidney dysfunction, stroke, neuropathy, coagulopathy, and uteroplacental insufficiency (Table 1).
- A diagnosis of preeclampsia is made when hypertension

occurring at or after 20 weeks of gestation is accompanied by any of the above disorders. When chronic kidney disease occurring before pregnancy or within less than 20 weeks of gestation or chronic hypertension in pregnancy is complicated by these organ damages, superimposed preeclampsia is diagnosed. Preeclampsia (including superimposed preeclampsia) is diagnosed regardless of the presence/absence of proteinuria. When these organ damages are present, severe preeclampsia (including superimposed preeclampsia) is diagnosed even if blood pressure is within the mild range, and careful management of the mother and the child is required.

- When examining a patient for the presence of organ damage, it is necessary to carefully determine whether the damage is attributable to aggravation of the preexisting condition or another disease.
- The condition should not be determined by a single examination. Instead, its course should be followed carefully to monitor for progressive worsening.

Definition of liver dysfunction without underlying disease

Key points

- The following description has been added to the diagnostic criteria for preeclampsia: “liver dysfunction (elevation of hepatic enzymes [ALT or AST > 40 IU/L] without underlying disease; severe persistent right hypochondriac or epigastric pain not responding to treatment and not attributable to other diagnoses)”. The most important aspect of considering this issue is the physiological changes that pregnancy imposes on the liver. Secondly, it is necessary to determine whether liver dysfunction, right hypochondriac pain, or epigastric pain, if any of these findings is present, is a symptom characteristic of pregnancy (gestational symptom) or a symptom present in a non-pregnant state (non-gestational symptoms).
- Liver disease reportedly occurs in less than 3% of all pregnancies¹⁾. The incidence of gestational liver disease is specific to the gestational period, but non-gestational disease can occur at any time.

What is progressive renal impairment?

Key points

- Progressive renal impairment is a case in which renal disorder is absent in early pregnancy, but renal function is reduced (shows deterioration) at or after 20 weeks of gestation, resulting in a serum creatinine (Cr) level of 1.0 mg/dl or more with other renal diseases excluded.
- Chronic kidney disease (CKD) in pregnancy should be managed with reference to the classification of CKD

severity.

Diagnosis and evaluation of proteinuria

Key points

- In principle, making a definitive diagnosis of proteinuria requires quantitative testing.
- 1. Detection of a urinary protein level of at least 300 mg/day in 24-h urine collection by Esback or other methods.
- 2. Protein/creatinine (P/C) ratio of 0.3 mg/mg·Cr or higher in spot urine samples.
- * A stricter criterion, 0.27 mg/mg·Cr or higher, is prescribed in the Guideline for Obstetric Practice in Japan 2017.

When quantitative testing is not feasible, proteinuria may be diagnosed when 2 or more consecutive test results of urinary protein 1+ or more are obtained by qualitative testing of spot urine samples using paper test strips.

Central nervous system (CNS) damage: brain and nerve damage (clonic convulsion, eclampsia, visual field disturbance, headache excluding primary headache)

Key points

- Eclampsia specified as a disease type of PIH in the previous classification has been deleted from the current revision, and is positioned as a form of CNS damage (brain and nerve damage) among organ damages associated with HDP.
- HDP-related organ diseases include severe headache and clonic convulsion as predictive signs of eclampsia and cortical blindness (visual field disturbance) due to the state of eclampsia affecting the occipital lobe.
- CNS damage (e.g., cerebral hemorrhage, cerebral infarction, subarachnoid hemorrhage) associated with hypertension during pregnancy or delivery or after delivery is also dealt with as a form of CNS damage. When stroke or cerebral sinus thrombosis occurs concomitantly with hypertension in pregnant, parturient, or puerperal women in relation to arteriovenous malformation or moyamoya disease, they are also regarded as CNS damage.
- Visual field disturbance may be observed in occipital lobe leukoencephalopathy, but is not a form of CNS damage when it is associated with a retinal lesion such as serous retinal detachment.
- Cerebral hemorrhage due to cerebral arteriovenous malformation not accompanied by hypertension is not regarded as CNS damage in HDP, but should be reported as pregnancy-related stroke or pregnancy-associated stroke.

Diagnosis of coagulopathy

Key points

- Coagulopathy is defined by thrombocytopenia (less than $150,000/\text{mm}^3$), disseminated intravascular coagulation (DIC), or hemolysis.
- HELLP syndrome (Hemolysis, Elevated Liver enzymes, and Low Platelet count) is dealt with separately from preeclampsia (including superimposed preeclampsia).
- Diagnostic criteria values for organ damage in HDP are different from those of HELLP syndrome.

Definition and diagnosis of fetal growth restriction (FGR) and the method of diagnosing umbilical arterial blood flow wave abnormality

Key points

- Fetal growth restriction (FGR) is defined by ultrasonographically estimated fetal weight less than -1.5 SD of the reference value.
- The diagnosis of FGR is determined by prospective assessment during pregnancy, and not by birth weight.
- The reference values of fetal weight by gestational week announced by the Japan Society of Ultrasonics in Japan or reported by the Perinatology Committee of the Japan Society of Obstetrics and Gynecology are used as fetal growth reference values.
- Uteroplacental insufficiency is diagnosed comprehensively by FGR, umbilical arterial blood flow wave abnormality, or stillbirth.

What is chronic hypertension?

Key points

- Chronic hypertension (CH) is defined as the presence of hypertension before pregnancy or before 20 weeks of gestation not accompanied by superimposed preeclampsia.
- Hypertension is diagnosed when the systolic BP is at least 140 mmHg or when the diastolic BP is at least 90 mmHg.
- Chronic hypertension includes normotension on antihypertensive therapy and spontaneous BP decrease in pregnant hypertensives, but does not include white coat hypertension and masked hypertension.
- When hypertension becomes increasingly severe in pregnant women with chronic hypertension, the condition remains in the category of chronic hypertension as long as there is no superimposed preeclampsia.

Management of chronic hypertension

Key points

- According to the current revision of the definition and classification, chronic hypertension in pregnancy has been classified as a type of HDP. However, there is no alteration in the management guideline for chronic hypertension.

White coat hypertension and masked hypertension

Key points

- If high office BP ($\geq 140/90$ mmHg) is found

when pregnant women undergo health screening, home BP measurement should be performed to distinguish between chronic hypertension and white coat hypertension.

- In general, white coat hypertension is defined by high BP ($\geq 140/90$ mmHg) in office settings and less than 135/85 mmHg in at-home or other out-of-office settings. Hypertension should be suspected when home BP is 135/85 mmHg or higher.
- White coat hypertension is not included in chronic hypertension according to the classification of HDP types.