中文題目：比較依抗藥性基因與依抗生素敏感性引導之療法在幽門螺旋桿菌第一線治療之療效- 一項多中心之隨機分派臨床試驗

英文題目：Comparison of genotypic resistance guided versus susceptibility testing guided therapy for the first-line eradication of *H. pylori*- a multicenter randomized trial

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前言(Background): The point mutations of 23S rRNA and gyrase A were reported to be associated with clarithromycin and levofloxacin resistance. However, whether genotypic resistance guided therapy is non-inferior to susceptibility testing guided therapy in eradication in first-line *H. pylori* infection remains uncertain. Therefore, we conducted a multi-center, open labeled, randomized controlled trial in Taiwan to compare the efficacy of genotypic resistance guided therapy versus susceptibility testing guided therapy in the first-line treatment for H. pylori infection.

材料及方法(Materials and Methods): Eligible patients were allocated 1:1 to receive either genotypic resistance-guided therapy or susceptibility testing-guided therapy. Agar dilution test was used to determine the minimum inhibitory concentrations of clarithromycin and levofloxacin. The 23S rRNA and gyrase A mutations were determined by polymerase chain reaction and direct sequencing.) In the group of genotypic resistance guided therapy**,** patients were treated with 14-day clarithromycin based sequential therapy containing esomeprazole 40mg and amoxicillin 1g for 7 days, followed by esomeprazole 40mg, clarithromycin 500mg and metronidazole 500mg for another 7 days in the absence of 23S rRNA (ribosomal RNA) mutation. In the presence of 23S rRNA mutation but the absence of gyrase A mutation, patients were treated with 14-day levofloxacin based sequential therapy containing esomeprazole 40mg and amoxicillin 1g for 7 days, followed by esomeprazole 40mg, levofloxacin 250mg and metronidazole 500mg for another 7 days. All of the above drugs were used twice a day. In the presence of both 23S rRNA and gyrase A mutations or failure of genotyping tests, bismuth quadruple therapy with esomeprazole 40mg twice daily, metronidazole 500mg three times daily, bismuth tripotassium dicitrate 300 mg (KCB F.C. Tablets; Swiss Pharm, Taiwan) and tetracycline 500mg four times daily were given for 10 days. In the group of susceptibility testing guided therapy, clarithromycin based sequential therapy for 14 days was given in the absence of clarithromycin resistance. In the presence of clarithromycin resistance but the absence of levofloxacin resistance, levofloxacin based sequential therapy for 14 days was given. In the presence of both clarithromycin and levofloxacin resistance or failure of *H. pylori* culture, bismuth quadruple therapy for 10 days was given. The ^{13}C-urea breath test was measured 6

weeks after treatment to assess *H. pylori* status. Eradication efficacy and adverse effects were assessed according to Intent-to-treat (ITT) and per protocol (PP) analyses. This trial was registered with ClinicalTrials.gov, NCT03556254.

結果(Results): A total of 560 eligible treatment-naive patients of *H. pylori* infection were randomly assigned to two treatment groups. The primary resistance rates of clarithromycin, levofloxacin, metronidazole, amoxicillin, tetracycline, 23S rRNA mutations and gyrase A mutation were 16·1% versus 21·1%, 20·7% versus 17·9%, 21·9% versus 25·5%, 2·9% versus 1·6%, 5·4% versus 6·0%, 17·7% versus 22·8%, and 19·9% versus 18·9% in genotypic resistance-guided therapy and susceptibility testing-guided therapy group, respectively. Using a non-inferiority trial design with a margin of 5%, eradication rates in genotypic resistance-guided therapy group and susceptibility testing-guided therapy group were 86·1% (95% CI: 81·5%-89·9%) versus 86·8% (95% CI: 82·3%-90·5%) in the ITT analysis (non-inferiority p-value=0·071), and 90·6% (95% CI: 86·4%-93·8%) versus 91·6% (95% CI: 87·6%-94·7%) in PP analysis (non-inferiority p-value=0·059), respectively. The side effects and percentages of antimicrobial resistance were similar in both groups.

結論 (Conclusion): Genotypic resistance guided therapy is not inferior to susceptibility testing (phenotypic resistance) guided therapy in the first-line treatment of *H. pylori* infection.

Keywords: *H. pylori*, resistance, genotypic, susceptibility testing, first-line