

DAFTAR PUSTAKA

- Ahmad M, Mehta P, Reddivari AKR, et al. (2020). *Percutaneous Coronary Intervention*. StatPearls Publishing.
- Akkaif, M. A., Daud, N. A. A., Sha'aban, A., Ng, M. L., Abdul Kader, M. A. S., Noor, D. A. M., & Ibrahim, B. (2021). The role of genetic polymorphism and other factors on clopidogrel resistance (Cr) in an asian population with coronary heart disease (chd). *Molecules*, 26(7).
<https://doi.org/10.3390/molecules26071987>
- Akutsu, N., Hori, K., Mizobuchi, S., Ogaku, A., Koyama, Y., Fujito, H., Arai, R., Ebuchi, Y., Migita, S., Morikawa, T., Tamaki, T., Kojima, K., Murata, N., Nishida, T., Kitano, D., Fukamachi, D., & Okumura, Y. (2022). Clinical Importance of the LDL-C/Apolipoprotein B Ratio for Neointimal Formation after Everolimus-Eluting Stent Implantations. *Journal of Atherosclerosis and Thrombosis*, 29(4), 536–550.
<https://doi.org/10.5551/jat.60954>
- Aleil, B., Jacquemin, L., De Poli, F., Zaehringer, M., Collet, J.-P., Montalescot, G., Cazenave, J.-P., Dickele, M.-C., Monassier, J.-P., & Gachet, C. (2008). Clopidogrel 150 mg/day to Overcome Low Responsiveness in Patients Undergoing Elective Percutaneous Coronary Intervention: Results From the VASP-02 (Vasodilator-Stimulated Phosphoprotein-02) Randomized Study. *JACC: Cardiovascular Interventions*, 1(6), 631–638.
<https://doi.org/https://doi.org/10.1016/j.jcin.2008.09.004>

Alraies, M. C., Darmoch, F., Tummala, R., & Waksman, R. (2017).

Diagnosis and management challenges of in-stent restenosis in coronary arteries. *World Journal of Cardiology*, 9(8), 640–651.
<https://doi.org/10.4330/wjc.v9.i8.640>

Angiolillo, D. J., Capranzano, P., Goto, S., Aslam, M., Desai, B., Charlton, R. K., Suzuki, Y., Box, L. C., Shoemaker, S. B., Zenni, M. M., Guzman, L. A., & Bass, T. A. (2008). A randomized study assessing the impact of cilostazol on platelet function profiles in patients with diabetes mellitus and coronary artery disease on dual antiplatelet therapy: results of the OPTIMUS-2 study. *European Heart Journal*, 29(18), 2202–2211. <https://doi.org/10.1093/eurheartj/ehn287>

Badan Penelitian dan Pengembangan Kesehatan. (2013). Riset Kesehatan Dasar 2013. *Riset Kesehatan Dasar 2013*.

Badan Penelitian dan Pengembangan Kesehatan. (2018).
Laporan_Nasional_RKD2018_FINAL.pdf. In *Badan Penelitian dan Pengembangan Kesehatan* (p. 198).

http://labdata.litbang.kemkes.go.id/images/download/laporan/RKD/2018/Laporan_Nasional_RKD2018_FINAL.pdf

Bagyura, Z., Kiss, L., Hirschberg, K., Berta, B., Széplaki, G., Lux, Á., Szelid, Z., Soós, P., & Merkely, B. (2017). Association between VEGF Gene Polymorphisms and In-Stent Restenosis after Coronary Intervention Treated with Bare Metal Stent. *Disease Markers*, 2017(Mehran I). <https://doi.org/10.1155/2017/9548612>

- Balli, M., Taşolar, H., Çetin, M., Tekin, K., Çağlıyan, E., Türkmen, S., Yilmaz, M., Elbasan, Z., Şahin, D. Y., & Çaylı, M. (2015). Use of the neutrophil to lymphocyte ratio for prediction of in-stent restenosis in bifurcation lesions. *European Review for Medical and Pharmacological Sciences*, 19(10), 1866–1873.
- Banning, A. P., Hood, K. L., Finn, A. V., Patterson, C., Abizaid, A., Eppihimer, M. J., Dawkins, K. D., & Baim, D. S. (2010). Differential Drug-eluting Stent Effects in Patients with Diabetes – Bench-to-bedside Evidence for Neointimal Suppression and Restenosis Reduction. *Interventional Cardiology Review*, 5(1), 27.
<https://doi.org/10.15420/icr.2010.5.1.27>
- Bergheanu, S. C., Pons, D., Karalis, I., Özsoy, O., Verschuren, J. J. W., Ewing, M. M., Quax, P. H. A., & Jukema, J. W. (2010). Genetic determinants of adverse outcome (restenosis, malapposition and thrombosis) after stent implantation. *Interventional Cardiology*, 2(2), 147–157. <https://doi.org/10.2217/ica.10.9>
- Buccheri, D., Piraino, D., Andolina, G., & Cortese, B. (2016). Understanding and managing in-stent restenosis: A review of clinical data, from pathogenesis to treatment. In *Journal of Thoracic Disease*.
<https://doi.org/10.21037/jtd.2016.10.93>
- Cai, N., Li, C., Gu, X., Zeng, W., Zhong, J., Liu, J., Zeng, G., Zhu, J., & Hong, H. (2023). CYP2C19 loss-of-function is associated with increased risk of hypertension in a Hakka population: a case-control

- study. *BMC Cardiovascular Disorders*, 23(1), 185.
<https://doi.org/10.1186/s12872-023-03207-w>
- Cassese, S., Byrne, R. A., Tada, T., Pinieck, S., Joner, M., Ibrahim, T., King, L. A., Fusaro, M., Laugwitz, K.-L., & Kastrati, A. (2014). Incidence and predictors of restenosis after coronary stenting in 10 004 patients with surveillance angiography. *Heart (British Cardiac Society)*, 100(2), 153–159. <https://doi.org/10.1136/heartjnl-2013-304933>
- Collet, J.-P., Hulot, J.-S., Pena, A., Villard, E., Esteve, J.-B., Silvain, J., Payot, L., Brugier, D., Cayla, G., Beygui, F., Bensimon, G., Funck-Brentano, C., & Montalescot, G. (2009). Cytochrome P450 2C19 polymorphism in young patients treated with clopidogrel after myocardial infarction: a cohort study. *Lancet (London, England)*, 373(9660), 309—317. [https://doi.org/10.1016/s0140-6736\(08\)61845-0](https://doi.org/10.1016/s0140-6736(08)61845-0)
- Cuisset, T., Frere, C., Quilici, J., Barbou, F., Morange, P. E., Hovasse, T., Bonnet, J.-L., & Alessi, M.-C. (2006). High post-treatment platelet reactivity identified low-responders to dual antiplatelet therapy at increased risk of recurrent cardiovascular events after stenting for acute coronary syndrome. *Journal of Thrombosis and Haemostasis : JTH*, 4(3), 542–549. <https://doi.org/10.1111/j.1538-7836.2005.01751.x>
- Farooq, V., Gogas, B. D., & Serruys, P. W. (2011). Restenosis: delineating the numerous causes of drug-eluting stent restenosis. *Circulation. Cardiovascular Interventions*, 4(2), 195–205.

<https://doi.org/10.1161/CIRCINTERVENTIONS.110.959882>

- Galeazzi, R., Olivieri, F., Spazzafumo, L., Rose, G., Montesanto, A., Giovagnetti, S., Cecchini, S., Malatesta, G., Di Pillo, R., & Antonicelli, R. (2018). Clustering of ABCB1 and CYP2C19 Genetic Variants Predicts Risk of Major Bleeding and Thrombotic Events in Elderly Patients with Acute Coronary Syndrome Receiving Dual Antiplatelet Therapy with Aspirin and Clopidogrel. *Drugs and Aging*, 35(7), 649–656. <https://doi.org/10.1007/s40266-018-0555-1>
- Ganesh, S. K., & Nabel, E. G. (2005). Genomics of in-stent restenosis: Early insights into a complex disease. *Circulation*, 112(16), 2378–2379. <https://doi.org/10.1161/CIRCULATIONAHA.105.574780>
- Grech, E. D. (2003). ABC of interventional cardiology: percutaneous coronary intervention. II: the procedure. *BMJ (Clinical Research Ed.)*, 326(7399), 1137–1140. <https://doi.org/10.1136/bmj.326.7399.1137>
- Haybar, H., Pezeshki, S. M. S., & Saki, N. (2020). Platelets in In-stent Restenosis: From Fundamental Role to Possible Prognostic Application. *Current Cardiology Reviews*, 16(4), 285–291. <https://doi.org/10.2174/1573403X15666190620141129>
- Her, A. Y., & Shin, E. S. (2018). Current Management of In-Stent Restenosis. *Korean Circulation Journal*, 48(5), 337–349. <https://doi.org/10.4070/kcj.2018.0103>
- Hu, R. T., Liu, J., Zhou, Y., & Hu, B. L. (2015). Association of smoking with restenosis and major adverse cardiac events after coronary stenting:

- A meta-analysis. *Pakistan Journal of Medical Sciences*, 31(4), 1002–1008. <https://doi.org/10.12669/pjms.314.7495>
- Hussein, A., Awad, M. S., Sabra, A. M., & Mahmoud, H. E. M. (2021). Anemia is a novel predictor for clinical ISR following PCI. *Egyptian Heart Journal*, 73(1), 4–9. <https://doi.org/10.1186/s43044-021-00163-8>
- Jaitner, J., Morath, T., Byrne, R. A., Braun, S., Gebhard, D., Bernlochner, I., Schulz, S., Mehilli, J., Schömig, A., Koch, W., Kastrati, A., & Sibbing, D. (2012). No association of ABCB1 C3435T genotype with clopidogrel response or risk of stent thrombosis in patients undergoing coronary stenting. *Circulation: Cardiovascular Interventions*, 5(1), 82–88.
<https://doi.org/10.1161/CIRCINTERVENTIONS.111.965400>
- Jeong, Y. H., Tantry, U. S., Kim, I. S., Koh, J. S., Kwon, T. J., Park, Y., Hwang, S. J., Bliden, K. P., Kwak, C. H., Hwang, J. Y., & Gurbel, P. A. (2011). Effect of CYP2C19 *2 and *23 loss-of-function alleles on platelet reactivity and adverse clinical events in East Asian acute myocardial infarction survivors treated with clopidogrel and aspirin. *Circulation: Cardiovascular Interventions*, 4(6), 585–594.
<https://doi.org/10.1161/CIRCINTERVENTIONS.111.962555>
- Kai Yin MD, D. K. A. P. (2014). Gene therapy for in-stent restenosis: Targets and delivery system. *Curr Res Cardiol* 2014;1(2):93-101, 1(2), 93–101.

Kang, Y., Lao, H., Yu, X., Chen, J., & Zhong, S. (2012). [Progress in genetic and epigenetic research on in-stent restenosis after percutaneous coronary interventions]. *Zhonghua yi xue yi chuan xue za zhi = Zhonghua yixue yichuanxue zazhi = Chinese journal of medical genetics*, 29(1), 38–42.

<https://doi.org/10.3760/cma.j.issn.1003-9406.2012.01.010>

Kern, M. J., Sorajja, P., & Lim, M. J. (2017). *The interventional cardiac catheterization handbook*.

Knuuti, J., Wijns, W., Saraste, A., Capodanno, D., Barbato, E., Funck-Brentano, C., Prescott, E., Storey, R. F., Deaton, C., Cuisset, T., Agewall, S., Dickstein, K., Edvardsen, T., Escaned, J., Gersh, B. J., Svitil, P., Gilard, M., Hasdai, D., Hatala, R., ... Group, E. S. C. S. D. (2019). 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). *European Heart Journal*, 41(3), 407–477.

<https://doi.org/10.1093/eurheartj/ehz425>

L'Allier, P. L., Ducrocq, G., Pranno, N., Noble, S., Ibrahim, R., Grégoire, J. C., Azzari, F., Nozza, A., Berry, C., Doucet, S., Labarthe, B., Thérioux, P., Tardif, J.-C., & null null. (2008). Clopidogrel 600-Mg Double Loading Dose Achieves Stronger Platelet Inhibition Than Conventional Regimens. *Journal of the American College of Cardiology*, 51(11), 1066–1072.

<https://doi.org/10.1016/j.jacc.2007.12.013>

- Lee, H. F., Cheng, Y. W., Peng, J. R., Hsu, C. Y., Yang, C. H., Chan, Y. H., & Chu, P. H. (2021). Impact of chronic kidney disease on long-term outcomes for coronary in-stent restenosis after drug-coated balloon angioplasty. *Journal of Cardiology*, 78(6), 564–570.
<https://doi.org/10.1016/j.jcc.2021.08.010>
- Lee, M. S., & Banka, G. (2016). In-stent Restenosis. *Interventional Cardiology Clinics*, 5(2), 211–220.
<https://doi.org/10.1016/j.iccl.2015.12.006>
- Lima-Filho, M. O., Figueiredo, G. L., Foss-Freitas, M. C., Foss, M. C., & Marin-Neto, J. A. (2010). Predictors of restenosis after percutaneous coronary intervention using bare-metal stents: a comparison between patients with and without dysglycemia. *Brazilian Journal of Medical and Biological Research = Revista Brasileira de Pesquisas Medicas e Biologicas*, 43(6), 572–579. <https://doi.org/10.1590/s0100-879x2010007500051>
- Mehilli, J., Kastrati, A., Bollwein, H., Dibra, A., Schühlen, H., Dirschinger, J., & Schömig, A. (2003). Gender and restenosis after coronary artery stenting. *European Heart Journal*, 24(16), 1523–1530.
[https://doi.org/10.1016/s0195-668x\(03\)00320-8](https://doi.org/10.1016/s0195-668x(03)00320-8)
- Miftahussurur, M., Doohan, D., Syam, A. F., Nusi, I. A., Subsomwong, P., Waskito, L. A., Maulahela, H., Akil, F., Uwan, W. B., Siregar, G., Fauzia, K. A., Rezkitha, Y. A. A., Rahman, A., Wibawa, I. D. N., Saudale, A. M. J., Ricardo, M., Sugihartono, T., Chomariyati, A.,

Bramantoro, T., ... Yamaoka, Y. (2021). Cyp2c19 polymorphisms in indonesia: Comparison among ethnicities and the association with clinical outcomes. *Biology*, 10(4), 1–12.
<https://doi.org/10.3390/biology10040300>

Minacapelli, A., Piraino, D., Buccheri, D., & Cortese, B. (2018). Drug-coated balloons for the treatment of in-stent restenosis in diabetic patients: A review of currently available scientific data. *Catheterization and Cardiovascular Interventions : Official Journal of the Society for Cardiac Angiography & Interventions*, 92(1), E20–E27. <https://doi.org/10.1002/ccd.26957>

Mohan, S., & Dhall, A. (2010). A comparative study of restenosis rates in bare metal and drug-eluting stents. *International Journal of Angiology*, 19(2). <https://doi.org/10.1055/s-0031-1278368>

Monraats, P. S., Pires, N. M. M., Agema, W. R. P., Zwinderman, A. H., Schepers, A., De Maat, M. P. M., Doevedans, P. A., De Winter, R. J., Tio, R. A., Waltenberger, J., Frants, R. R., Quax, P. H. A., Van Vlijmen, B. J. M., Atsma, D. E., Van Der Laarse, A., Van Der Wall, E., & Jukema, J. W. (2005). Genetic inflammatory factors predict restenosis after percutaneous coronary interventions. *Circulation*, 112(16), 2417–2425.

<https://doi.org/10.1161/CIRCULATIONAHA.105.536268>

Na'im, A., & Syaputra, H. (2010). Kewarganegaraan, suku bangsa, agama, dan bahasa sehari-hari penduduk Indonesia. In

วารสารวิชาการมหาวิทยาลัยอีสเทิร์นแอดเชีย (Vol. 4, Issue 1).

O' Brien, E. R., Ma, X., Simard, T., Pourdjabbar, A., & Hibbert, B. (2011).

Pathogenesis of neointima formation following vascular injury.

Cardiovascular & Hematological Disorders Drug Targets, 11(1), 30–

39. <https://doi.org/10.2174/187152911795945169>

Pintaningrum, Y., . V., Dewi, I. P., Putra, H. B. P., Mappangara, I., Amir,

M., Yusuf, I., & Bukhari, A. (2022). CYP2C19 polymorphism and

coronary in-stent restenosis: A systematic review and meta-analysis.

F1000Research, 11, 346.

<https://doi.org/10.12688/f1000research.109321.2>

Rahmany, Z. M., Pintaningrum, Y., Ermawan, R., Kementerian, L., &

Republik, K. (2020). *Hubungan Lama Implantasi Stent Dengan*

Kejadian in-Stent Restenosis. 10(1), 355–363.

Rytkin, E., Mirzaev, K. B., Grishina, E. A., Smirnov, V. V., Ryzhikova, K.

A., Sozaeva, Z. A., Gililarov, M. I., Andreev, D. A., & Sychev, D. A.

(2017). Do CYP2C19 and ABCB1 gene polymorphisms and low

CYP3A4 isoenzyme activity have an impact on stent implantation

complications in acute coronary syndrome patients?

Pharmacogenomics and Personalized Medicine, 10, 243–245.

<https://doi.org/10.2147/PGPM.S143250>

Sajadian, M., Alizadeh, L., Ganjifard, M., Mardani, A., Ansari, M., &

Falsoleiman, H. (2018). Factors Affecting in-stent Restenosis in

Patients Undergoing Percutaneous Coronary Angioplasty. *Galen*

Medical Journal, 7(e961).

Sanchis-Gomar, F., Perez-Quilis, C., Leischik, R., & Lucia, A. (2016).

Epidemiology of coronary heart disease and acute coronary syndrome. *Annals of Translational Medicine*, 4(13), 1–12.

<https://doi.org/10.21037/atm.2016.06.33>

Seiji Hokimoto, Michio Mizobe, Tadasuke Chitose, Kenichi Tsujita, Koichi Kaikita, Kazuko Nakagawa, and H. O. (2011). Impact of CYP2C19 Polymorphism on In-Stent Restenosis in Patients With Drug-Eluting Stent Implantation. *Circulation*, 124(suppl_21).

Shim, C. Y., Yoon, S.-J., Park, S., Kim, J.-S., Choi, J. R., Ko, Y.-G., Choi, D., Ha, J.-W., Jang, Y., Chung, N., Shim, W.-H., & Cho, S.-Y. (2009).

The clopidogrel resistance can be attenuated with triple antiplatelet therapy in patients undergoing drug-eluting stents implantation.

International Journal of Cardiology, 134(3), 351–355.

<https://doi.org/10.1016/j.ijcard.2008.02.016>

Shlofmitz, E., Iantorno, M., & Waksman, R. (2019). Restenosis of Drug-Eluting Stents: A New Classification System Based on Disease Mechanism to Guide Treatment and State-of-The-Art Review. *Circulation: Cardiovascular Interventions*, 12(8), 1–8.

<https://doi.org/10.1161/CIRCINTERVENTIONS.118.007023>

Storey, R. F., Thornton, S. M., Lawrence, R., Husted, S., Wickens, M., Emanuelsson, H., Cannon, C. P., Heptinstall, S., & Armstrong, M. (2009). Ticagrelor yields consistent dose-dependent inhibition of ADP-

induced platelet aggregation in patients with atherosclerotic disease regardless of genotypic variations in P2RY12, P2RY1, and ITGB3. *Platelets*, 20(5), 341–348.

<https://doi.org/10.1080/09537100903075324>

Subbotin, V. M. (2012). Neovascularization of coronary tunica intima (DIT) is the cause of coronary atherosclerosis. Lipoproteins invade coronary intima via neovascularization from adventitial vasa vasorum, but not from the arterial lumen: A hypothesis. *Theoretical Biology and Medical Modelling*, 9(1), 1. <https://doi.org/10.1186/1742-4682-9-11>

Tamhane, U., Meier, P., Chetcuti, S., Chen, K.-Y., Rha, S.-W., Grossman, M. P., & Gurm, H. (2009). Efficacy of cilostazol in reducing restenosis in patients undergoing contemporary stent based PCI: a meta-analysis of randomised controlled trials. *EuroIntervention : Journal of EuroPCR in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology*, 5(3), 384–393.

<https://doi.org/10.4244/v5i3a60>

Tang, X., Wang, J., & Zhang, J. (2012). *Effect of the CYP2C19 * 2 and * 3 genotypes , ABCB1 C3435T and PON1 Q192R alleles on the pharmacodynamics and adverse clinical events of clopidogrel in Chinese people after percutaneous coronary intervention.*

<https://doi.org/10.1007/s00228-012-1446-8>

Torrado, J., Buckley, L., Durán, A., Trujillo, P., Toldo, S., Valle Raleigh, J., Abbate, A., Biondi-Zoccaí, G., & Guzmán, L. A. (2018). Restenosis,

Stent Thrombosis, and Bleeding Complications: Navigating Between Scylla and Charybdis. *Journal of the American College of Cardiology*, 71(15), 1676–1695.

<https://doi.org/https://doi.org/10.1016/j.jacc.2018.02.023>

Trenk, D., Hochholzer, W., Fromm, M. F., Chialda, L.-E., Pahl, A., Valina, C. M., Stratz, C., Schmiebusch, P., Bestehorn, H.-P., Büttner, H. J., & Neumann, F.-J. (2008). Cytochrome P450 2C19 681G>A polymorphism and high on-clopidogrel platelet reactivity associated with adverse 1-year clinical outcome of elective percutaneous coronary intervention with drug-eluting or bare-metal stents. *Journal of the American College of Cardiology*, 51(20), 1925–1934.

<https://doi.org/10.1016/j.jacc.2007.12.056>

Uchiyama, S. (2011). Clopidogrel Resistance: Identifying and Overcoming a Barrier to Effective Antiplatelet Treatment. *Cardiovascular Therapeutics*, 29(6), e100–e111.

<https://doi.org/https://doi.org/10.1111/j.1755-5922.2010.00202.x>

Waksman, R., & Steinviel, A. (2016). In-Stent Restenosis? *Circulation. Cardiovascular Interventions*, 9(e004150), 1–3.

<https://doi.org/10.1056/NEJMra1210816.2>.

Wang, P., Qiao, H., Wang, R. J., Hou, R., & Guo, J. (2020). The characteristics and risk factors of in-stent restenosis in patients with percutaneous coronary intervention: what can we do. *BMC Cardiovascular Disorders*, 20(1), 1–6. <https://doi.org/10.1186/s12872-020-01395-0>

020-01798-2

Wang, T., Zhao, T., Bao, S., Jia, L., Feng, J., Yu, A., Sun, L., Guo, X., Li, H., & Yu, L. (2020). CYP2C19, PON1, and ABCB1 gene polymorphisms in Han and Uygur populations with coronary artery disease in Northwestern Xinjiang, China, From 2014 Through 2019. *Medicine*, 99(29), e20582.

<https://doi.org/10.1097/MD.00000000000020582>

Wang, X. qin, Shen, C. lin, Wang, B. ning, Huang, X. hui, Hu, Z. le, & Li, J. (2015). Genetic polymorphisms of CYP2C19*2 and ABCB1 C3435T affect the pharmacokinetic and pharmacodynamic responses to clopidogrel in 401 patients with acute coronary syndrome. *Gene*, 558(2), 200–207. <https://doi.org/10.1016/j.gene.2014.12.051>

Wei, X., Zhang, Y., Yan, G., & Wang, X. (2021). The relationship between chronic kidney disease and the severity and long-term prognosis of patients with coronary artery disease after drug-eluting stent implantation. *International Journal of General Medicine*, 14, 399–404.

<https://doi.org/10.2147/IJGM.S295098>

Wilson, S., Mone, P., Kansakar, U., Jankauskas, S. S., Donkor, K., Adebayo, A., Varzideh, F., Eacobacci, M., Gambardella, J., Lombardi, A., & Santulli, G. (2022). Diabetes and restenosis. *Cardiovascular Diabetology*, 21(1), 1–14. <https://doi.org/10.1186/s12933-022-01460-5>

Wirth, F., Zahra, G., Xuereb, R. G., Barbara, C., Camilleri, L., Fenech, A., & Azzopardi, L. M. (2018). CYP2C19*2 Allele Carrier Status and

Coronary In-stent Restenosis: Is There an Association? *Journal of Exploratory Research in Pharmacology*, 3(2), 55–60.

<https://doi.org/10.14218/jerp.2018.00002>

Woolland, K. J. (2013). Immunological aspects of atherosclerosis. *Clinical Science (London, England : 1979)*, 125(5), 221–235.

<https://doi.org/10.1042/CS20120576>

Yusuf, I., Djojosubroto, M. W., Ikawati, R., Lum, K., Kaneko, A., & Marzuki, S. (2003). Ethnic and geographical distributions of CYP2C19 alleles in the populations of Southeast Asia. *Advances in Experimental Medicine and Biology*, 531, 37–46. https://doi.org/10.1007/978-1-4615-0059-9_3

Zhang, M., Wang, J., Zhang, Y., Zhang, P., Jia, Z., Ren, M., Jia, X., Ma, L., Gao, M., & Hou, Y. (2020). Impacts of CYP2C19 polymorphism and clopidogrel dosing on in-stent restenosis: A retrospective cohort study in Chinese patients. *Drug Design, Development and Therapy*, 14, 669–676. <https://doi.org/10.2147/DDDT.S242167>

Zheng, C., Kang, J., Park, K. W., Han, J. K., Yang, H. M., Kang, H. J., Koo, B. K., & Kim, H. S. (2019). The predictors of target lesion revascularization and rate of in-stent restenosis in the second-generation drug-eluting stent era. *Journal of Interventional Cardiology*, 2019. <https://doi.org/10.1155/2019/3270132>

Zholdybayeva, E. V., Talzhanov, Y. A., Aitkulova, A. M., Tarlykov, P. V., Kulmambetova, G. N., Iskakova, A. N., Dzholdasbekova, A. U.,

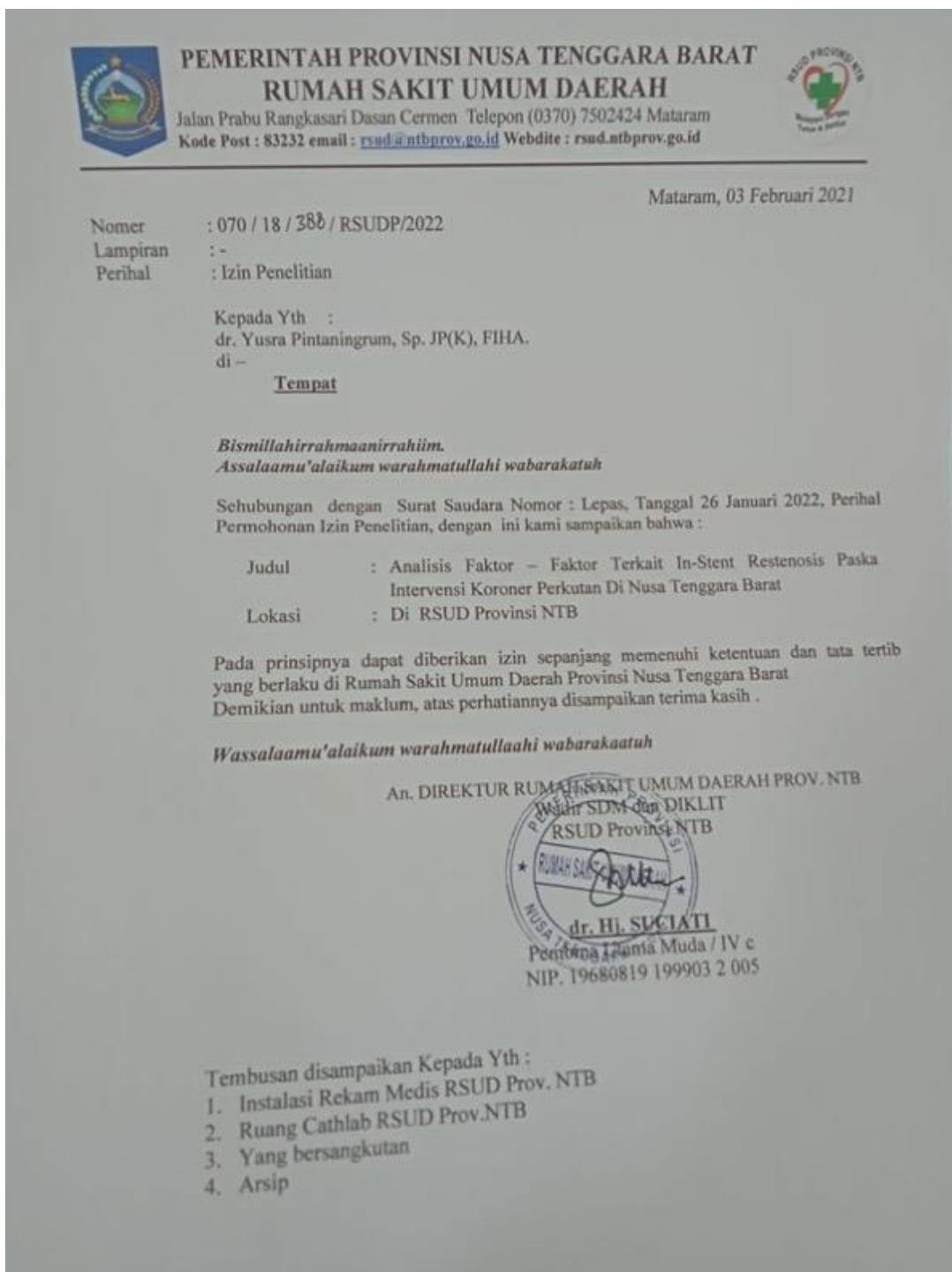
Visternichan, O. A., Taizhanova, D. Z., & Ramanculov, E. M. (2016).

Genetic risk factors for restenosis after percutaneous coronary intervention in Kazakh population. *Human Genomics*.

<https://doi.org/10.1186/s40246-016-0077-z>

DAFTAR LAMPIRAN

Lampiran 1: Surat rekomendasi persetujuan etik



Lampiran 2 : Lembar persetujuan sebagai responden



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LEMBAR PERSETUJUAN SEBAGAI RESPONDEN.

Kepada
Bapak/Ib/Sdr/I, calon responden
Di tempat

Dengan Hormat,
Saya Mahasiswa/Peneliti :
Nama : dr. Yusra Pintaningrum, SpJP(K),FIHA,FAPSC,FAsCC
NIM/NIDN/NIP : 197904262008122001

Bermaksud melakukan penelitian yang berjudul “ Pengaruh gen polimorfisme CYP2C19 pada instant restenosis signifikan paska intervensi koroner perkutan di RSUD Provinsi NTB”, dengan melibatkan Bapak / Ibu / Sdr / i sebagai responden selama 1 hari. Adapun tujuan penelitian ini adalah untuk menganalisis pengaruh faktor genetik *single nucleotide polymorphism* (SNP) CYP2C19 dengan *instant restenosis* pada pasien yang telah dilakukan intervensi koroner perkutan sebelumnya di RSUD Provinsi NTB, dan cara pengambilan data dilakukan dengan kuisioner dan pengambilan darah vena.

Segala informasi yang diberikan akan dijamin kerahasiaannya dan saya bertanggung jawab apabila informasi yang diberikan merugikan Bapak / Ibu / Srd/ I, maka dari itu tidak perlu mencantumkan nama atau identitas lainnya. Sehubungan dengan hal tersebut, apabila Bapak/Ibu/ Sdr/i, setuju untuk ikut serta dalam penelitian ini dimohon untuk menandatangani kolom yang telah disediakan. Dan jika terdapat hal – hal yang perlu diklarifikasi terkait pernyataan diatas, dapat langsung menghubungi peneliti No. Hp 08113907161.

Atas kesediaan dan kerjasamanya saya ucapan terimakasih.

Mataram, 24 Februari 2022
Responden

Peneliti

(.....)

(dr. Yusra Pintaningrum, SpJP(K),FIHA)

Saksi

(.....)

Lampiran 3: Case Report Form

No. Subjek :

DATA SUBJEK PENELITIAN

I. IDENTITAS PASIEN

- a. Nama :
b. Umur : tahun
c. Jenis Kelamin :
d. Suku responden :
Suku ayah responden :
Suku ibu responden :
e. Tingkat Pendidikan : SD / SMP / SMA / S1/S2 /S3*)
f. Alamat :
g. Nomor rekam medik :
h. Nomor telepon :
i. Tanggal pemeriksaan :

II. KELUHAN*

Sesak (1 bulan terakhir) :
sering / kadang-kadang / jarang/ tidak pernah*

Nyeri dada (1 bulan terakhir) :
sering / kadang-kadang / jarang/ tidak pernah*

III. POLA HIDUP

Merokok : ya / tidak
Jika merokok, berapa lama : tahun
Stop merokok sejak : tahun

IV. RIWAYAT PENYAKIT

- a. Hipertensi : ya / tidak
- b. Diabetes mellitus : ya / tidak

V. OBAT YANG DIKONSUMSI SAAT INI
(nama, dosis, dan frekuensi pemberian)

.....
.....
.....
.....
.....
.....
.....
.....
.....
.....
.....
.....
.....

VI. DATA ANTROPOMETRI SUBJEK (diambil dari
data pre-cath)

- a. Tinggi badan : cm
- b. Berat badan : kg
- c. Berat massa tubuh :
Catatan :
Rumus BMI = Berat badan
$$(tinggi badan)^2$$

Tinggi badan dalam meter (m)
Berat Badan dalam kilogram (kg)
- d. Status BMI : underweight / normal / overweight /
obesitas *)
Catatan :
< 18,5 : underweight
18,5-24,9 : normal
25-29,9 : overweight
>30 : obesitas

VII. PEMERIKSAAN ELEKTROKARDIOGRAFI
(EKG) :

.....

VIII. HASIL LABORATORIUM

Haemoglobin : g/dL
Leukosit : $10^3/\mu\text{L}$
Trombosit : $10^3/\mu\text{L}$
Neutrofil :
Limfosit :
Neutrofil/limfosit :
Kolesterol total : mg/dL
HDL : mg/dL
LDL : mg/dL
Triglicerida : mg/dL
Serum kreatinin : mg/dL
Apo B : mg/dL
CYP2C19 :(lingkari dibawah ini)...

*1/*1* : normal, extensive metabolizer

*1/*2 atau *1/*3 : intermediate metabolizer

*2/*2 atau *3/*3 atau *2/*3 : poor metabolizer

IX. PEMERIKSAAN ECHOCARDIOGRAFI

a. LVEF by teich:.....
b. E/A ratio :
c. LVIDD :
d. IVCT : ms
e. IVRT : ms
f. MVET : ms

X. KATETERISASI

a. Tanggal PCI I
.....
i. Lokasi : LAD/ LCX/ RCA*
ii. Jenis stent : DES / BMS*
iii. Nama stent
.....
..

- iv. Ukuran stent
.....
....
- b. Tanggal PCI II
.....
i. Lokasi : LAD/ LCX/ RCA *
ii. Jenis stent : DES / BMS *
iii. Nama stent
.....
....
- iv. Ukuran stent
.....
....
- c. Tanggal PCI III (bila ada)
.....
i. Lokasi : LAD/ LCX/ RCA*
ii. Jenis stent : DES / BMS*
iii. Nama stent
.....
....
- iv. Ukuran stent
.....
....

(bila dilakukan pemasangan stent di beberapa lokasi maka ditulis juga semua lokasi, jenis stent, dan ukurannya)

Catatan :

*) coret yang tidak perlu

Lampiran 4 : Hasil analisis statistik

1. Data Demografi Variabel Numerik

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Usia Responden	85	39	82	60.45	8.110
Hemoglobin (g/dl)	85	11.0	17.4	13.925	1.4687
Neutrofil/Limfosit	85	.9	29.2	2.863	3.2388
Kolesterol total (mg/dl)	85	83	276	166.73	41.913
HDL (mg/dl)	85	24	79	40.12	10.062
LDL (mg/dl)	85	36	222	109.45	38.927
Trigliserida (mg/dl)	85	40	527	139.84	82.414
Apo-B (mg/dl)	85	38	202	95.42	31.012
Valid N (listwise)	85				

2. Analisis bivariat hubungan antar variabel data kategorikal

2.1. Jenis Kelamin * In Stent Restenosis

Crosstab

Count

		In Stent Restenosis		Total
		> 50%	< 50%	
Jenis Kelamin	Laki-laki	14	60	74
	Perempuan	3	8	11
Total		17	68	85

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.418 ^a	1	.518		
Continuity Correction ^b	.059	1	.809		
Likelihood Ratio	.391	1	.532		
Fisher's Exact Test				.686	.382
Linear-by-Linear Association	.413	1	.521		
N of Valid Cases	85				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 2.20.

b. Computed only for a 2x2 table

2.2. Penggunaan Clopidogrel * In Stent Restenosis

Crosstab

Count

	Penggunaan Clopidogrel	In Stent Restenosis		Total
		> 50%	< 50%	
Tidak		3	6	9
Ya		14	62	76
Total		17	68	85

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.118 ^a	1	.290		
Continuity Correction ^b	.381	1	.537		
Likelihood Ratio	.998	1	.318		
Fisher's Exact Test				.375	.255
Linear-by-Linear Association	1.105	1	.293		
N of Valid Cases	85				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 1.80.

b. Computed only for a 2x2 table

2.3. Merokok * In Stent Restenosis

Crosstab

Count

	Merokok	In Stent Restenosis		Total
		> 50%	< 50%	
Tidak				
Ya		4	8	12
Total		13	60	73
		17	68	85

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.553 ^a	1	.213		
Continuity Correction ^b	.734	1	.392		
Likelihood Ratio	1.395	1	.238		
Fisher's Exact Test				.247	.191
Linear-by-Linear Association	1.534	1	.215		
N of Valid Cases	85				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 2.40.

b. Computed only for a 2x2 table

2.4. Hipertensi * In Stent Restenosis

Crosstab

Count

		In Stent Restenosis		Total
		> 50%	< 50%	
Hipertensi	Ya	10	32	42
	Tidak	7	36	43
Total		17	68	85

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.753 ^a	1	.386		
Continuity Correction ^b	.356	1	.551		
Likelihood Ratio	.756	1	.385		
Fisher's Exact Test				.427	.276
Linear-by-Linear Association	.744	1	.388		
N of Valid Cases	85				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 8.40.

b. Computed only for a 2x2 table

2.5. Diabetes Melitus * In Stent Restenosis

Crosstab

Count

		In Stent Restenosis		Total
		> 50%	< 50%	
Diabetes Melitus	Ya	4	15	19
	Tidak	13	53	66
	Total	17	68	85

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.017 ^a	1	.896		
Continuity Correction ^b	.000	1	1.000		
Likelihood Ratio	.017	1	.897		
Fisher's Exact Test				1.000	.563
Linear-by-Linear Association	.017	1	.897		
N of Valid Cases	85				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 3.80.

b. Computed only for a 2x2 table

2.6. Stage eGFR * In Stent Restenosis

Crosstab

Count

		In Stent Restenosis		Total
		> 50%	< 50%	
Stage eGFR	<60	11	30	41
	=60	6	38	44
	Total	17	68	85

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.309 ^a	1	.129		
Continuity Correction ^b	1.558	1	.212		
Likelihood Ratio	2.330	1	.127		
Fisher's Exact Test				.176	.106
Linear-by-Linear Association	2.282	1	.131		
N of Valid Cases	85				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 8.20.

b. Computed only for a 2x2 table

2.7. Kategori CYP2C19 * In Stent Restenosis

Crosstab

Count

		In Stent Restenosis		Total
		> 50%	< 50%	
Kategori CYP2C19	Loss of Function	15	41	56
	Wild-type Genotypes	2	27	29
Total		17	68	85

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4.724 ^a	1	.030		
Continuity Correction ^b	3.562	1	.059		
Likelihood Ratio	5.428	1	.020		
Fisher's Exact Test				.044	.025
Linear-by-Linear Association	4.668	1	.031		
N of Valid Cases	85				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 5.80.

b. Computed only for a 2x2 table

2.8. Genotip ABCB1 * In Stent Restenosis

Crosstab

Count	In Stent Restenosis		Total
	> 50%	< 50%	
Genotip ABCB1	AA	3	15
	AG	9	33
	GG	5	20
Total		17	68
			85

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.179 ^a	2	.915
Likelihood Ratio	.183	2	.912
Linear-by-Linear Association	.052	1	.819
N of Valid Cases	85		

a. 1 cells (16.7%) have expected count less than 5. The minimum expected count is 3.60.

2.9. Jenis Stent * In Stent Restenosis

Crosstab

Count	In Stent Restenosis		Total
	> 50%	< 50%	
Jenis Stent	BMS	8	7
	DES	9	61
Total		17	68
			85

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	12.649 ^a	1	.000		
Continuity Correction ^b	10.246	1	.001		
Likelihood Ratio	10.628	1	.001		
Fisher's Exact Test				.001	.001
Linear-by-Linear Association	12.500	1	.000		
N of Valid Cases	85				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 3.00.

b. Computed only for a 2x2 table

3. Analisis bivariat data numerik

Group Statistics

	In Stent Restenosis	N	Mean	Std. Deviation	Std. Error Mean
Usia Responden	> 50%	17	56.00	9.083	2.203
	< 50%	68	61.56	7.516	.911
Kolesterol total (mg/dl)	> 50%	17	169.47	60.428	14.656
	< 50%	68	166.04	36.442	4.419
HDL (mg/dl)	> 50%	17	38.76	6.760	1.639
	< 50%	68	40.46	10.745	1.303
LDL (mg/dl)	> 50%	17	114.41	56.571	13.720
	< 50%	68	108.21	33.582	4.072
Triglicerida (mg/dl)	> 50%	17	132.06	64.202	15.571
	< 50%	68	141.78	86.671	10.510
Apo-B (mg/dl)	> 50%	17	97.06	41.789	10.135
	< 50%	68	95.01	28.069	3.404

		Independent Samples Test								
		Levene's Test for Equality of Variances			t-test for Equality of Means					
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
Usia Responden	Equal variances assumed	.245	.622	-2.614	83	.011	-5.559	2.127	-9.788	-1.329
	Equal variances not assumed			-2.332	21.794	.029	-5.559	2.384	-10.506	-.612
Kolesterol total (mg/dl)	Equal variances assumed	15.239	.000	.300	83	.765	3.426	11.427	-19.302	26.155
	Equal variances not assumed			.224	19.004	.825	3.426	15.308	-28.612	35.465
HDL (mg/dl)	Equal variances assumed	1.488	.226	-.618	83	.539	-1.691	2.739	-7.138	3.756
	Equal variances not assumed			-.808	38.892	.424	-1.691	2.094	-5.927	2.545
LDL (mg/dl)	Equal variances assumed	14.444	.000	.586	83	.560	6.206	10.597	-14.871	27.283
	Equal variances not assumed			.434	18.908	.669	6.206	14.312	-23.759	36.171
Triglicerida (mg/dl)	Equal variances assumed	.335	.564	-.433	83	.666	-9.721	22.456	-54.385	34.944
	Equal variances not assumed			-.517	32.299	.608	-9.721	18.787	-47.974	28.532
Apo-B (mg/dl)	Equal variances assumed	5.207	.025	.242	83	.810	2.044	8.457	-14.776	18.864
	Equal variances not assumed			.191	19.753	.850	2.044	10.692	-20.276	24.364

4. Analisis multivariat hubungan antar variabel dengan ISR

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	gender(1)	.739	1.297	.324	1	.569
	penggunaanCPG(1)	3.850	1.612	5.706	1	.017
	merokok(1)	-1.077	1.280	.708	1	.400
	hipertensi(1)	2.441	1.185	4.242	1	.039
	DM(1)	-.140	1.101	.016	1	.899
	Stage(1)	3.025	1.421	4.532	1	.033
	CYP2C19(1)	3.260	1.581	4.253	1	.039
	ABCB1			4.253	2	.119
	ABCB1(1)	1.170	1.344	.758	1	.384
	ABCB1(2)	-2.764	1.639	2.845	1	.092
	jenisstent(1)	5.242	1.889	7.699	1	.006
	usia	.291	.112	6.784	1	.009
	Kolesteroltotal	-.077	.047	2.659	1	.103
	HDL	.153	.089	2.955	1	.086
	LDL	-.033	.063	.283	1	.594
	Triglicerida	.018	.012	2.300	1	.129
	ApoB	.180	.097	3.445	1	.063
	Constant	-32.888	12.685	6.722	1	.010
						.000

a. Variable(s) entered on step 1: gender, penggunaanCPG, merokok, hipertensi, DM, Stage, CYP2C19, ABCB1, jenisstent, usia, Kolesteroltotal, HDL, LDL, Triglicerida, ApoB.

4. Hubungan antara polimorfisme CYP2C19 terhadap pasien dengan hipertensi, jenis stent, penyakit ginjal dengan eGFR <60 dengan risiko terjadinya ISR.

4.1. Hipertensi, CYP2C19, ISR

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.563 ^a	1	.010		
Continuity Correction ^b	4.741	1	.029		
Likelihood Ratio	9.607	1	.002		
Fisher's Exact Test				.017	.009
Linear-by-Linear Association	6.406	1	.011		
N of Valid Cases	42				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 3.33.

b. Computed only for a 2x2 table

4.2. DES, CYP2C19, ISR

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.165 ^a	1	.280		
Continuity Correction ^b	.508	1	.476		
Likelihood Ratio	1.247	1	.264		
Fisher's Exact Test				.466	.243
Linear-by-Linear Association	1.148	1	.284		
N of Valid Cases	70				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 3.47.

b. Computed only for a 2x2 table

4.3. BMS, CYP2C19, ISR

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.637 ^a	1	.104		
Continuity Correction ^b	.744	1	.388		
Likelihood Ratio	3.404	1	.065		
Fisher's Exact Test				.200	.200
Linear-by-Linear Association	2.462	1	.117		
N of Valid Cases	15				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .93.

b. Computed only for a 2x2 table

4.4. e-GFR, CYP2C19, ISR

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.410 ^a	1	.121		
Continuity Correction ^b	1.333	1	.248		
Likelihood Ratio	2.795	1	.095		
Fisher's Exact Test				.233	.122
Linear-by-Linear Association	2.351	1	.125		
N of Valid Cases	41				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 2.95.

b. Computed only for a 2x2 table

5. Hubungan antara hipertensi, eGFR, CYP2C19 dengan ISR pada pasien yang diberikan ticagrelor

5.1. Analisis Multivariat

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a HT(1)	-.687	1.531	.202	1	.653	.503
eGFR(1)	-.687	1.531	.202	1	.653	.503
CYP2C19(1)	-1.055	1.744	.366	1	.545	.348
Constant	.687	1.812	.144	1	.704	1.989

5.2. Analisis Bivariat HT X ISR

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	.225 ^a	1	.635		
Continuity Correction ^b	.000	1	1.000		
Likelihood Ratio	.228	1	.633		
Fisher's Exact Test				1.000	.595
Linear-by-Linear Association	.200	1	.655		
N of Valid Cases	9				

5.3. Analisis Bivariat eGFR X ISR

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	.225 ^a	1	.635		
Continuity Correction ^b	.000	1	1.000		
Likelihood Ratio	.228	1	.633		
Fisher's Exact Test				1.000	.595
Linear-by-Linear Association	.200	1	.655		
N of Valid Cases	9				

5.4. Analisis Bivariat CYP2C19 X ISR

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	.321 ^a	1	.571		
Continuity Correction ^b	.000	1	1.000		
Likelihood Ratio	.309	1	.578		
Fisher's Exact Test				1.000	.583
Linear-by-Linear Association	.286	1	.593		
N of Valid Cases	9				