2.4.1 Faktor-faktor yang mempengaruhi kekakuan arteri padaDM tipe-2 .......................................................... 20
2.4.2 Pengukuran kekakuan arteri.............................................. 23
2.5 Neutrophil–Lymphocyte Ratio dan Kekakuan Arteri.............. 24
BAB 3 KERANGKA KONSEPTUAL DAN HIPOTESIS PENELITIAN.... 28
3.1 Kerangka Konseptual ........................................................... 28
3.2 Hipotesis Penelitian.............................................................. 30
BAB 4 METODE PENELITIAN................................................................. 31
4.1 Desain penelitian................................................................... 31
4.2 Tempat dan waktu penelitian .................................................. 31
4.3 Populasi dan sampel penelitian............................................... 31
4.3.1 Populasi penelitian............................................................... 31
4.3.2 Jenis data ........................................................................ 31
4.3.3 Sampel penelitian................................................................. 32
4.3.3.1 Kriteria inklusi .......................................................... 32
4.3.3.2 Kriteria eksklusi ........................................................ 32
4.3.3.3 Besar sampel ............................................................. 32
4.4 Variabel penelitian .................................................................. 33
4.5 Definisi operasional ................................................................. 33
4.5.1 DM tipe-2 ...................................................................... 33
4.5.2 NLR (Neutrophil-Lymphocyte Ratio) .................................... 34
4.5.3 Kekakuan arteri dan baPWV .............................................. 34
4.5.4 Hipertensi ...................................................................... 35
4.5.5 Merokok ........................................................................ 35
4.5.6 Infeksi ............................................................................ 35
4.5.7 CKD stage 5 .................................................................. 35
4.5.8 Keganasan ..................................................................... 36
4.6 Rencana pengolahan dan analisis data ...................................... 36
4.6.1 Pengumpulan data .............................................................. 36
4.6.2 Penyajian data ................................................................. 36
4.6.3 Analisis data penelitian .................................................... 36
4.7 Protokol Penelitian ................................................................. 38
BAB 5 HASIL PENELITIAN ................................................................. 39
5.1 Karakteristik subjek penelitian................................................ 39
5.2 Gambaran Neutrophil–Lymphocyte Ratio pada DM tipe-2 di Instalasi Rawat Jalan Poliklinik Endokrin Metabolisme RSUD Dr. Soetomo Surabaya................................................................. 42
5.3 Gambaran kekakuan arteri yang diukur dengan baPWV pada DM tipe-2 di Instalasi Rawat Jalan Poliklinik Endokrin Metabolisme RSUD Dr. Soetomo Surabaya................................................................. 43
5.4 Korelasi antara Neutrophil–Lymphocyte Ratio dengan Kekakuan Arteri (baPWV) pada DM tipe-2 di Instalasi Rawat Jalan Poliklinik Endokrin Metabolisme RSUD Dr. Soetomo Surabaya 45

BAB 6 PEMBAHASAN ........................................................................ 47
6.1 Karakteristik subjek penelitian................................................ 47
6.2 Gambaran Neutrophil–Lymphocyte Ratio pada DM Tipe-2 di Instalasi Rawat Jalan Poliklinik Endokrin Metabolisme RSUD Dr. Soetomo Surabaya................................................................. 51
6.3 Gambaran Kekakuan Arteri yang Dinilai dengan Ba-PWV pada DM Tipe-2 di Instalasi Rawat Jalan Poliklinik Endokrin Metabolisme RSUD Dr. Soetomo Surabaya................................................................. 52
6.4 Korelasi Antara Neutrophil–Lymphocyte Ratio dengan Kekakuan Arteri yang Diukur dengan Ba-PWV pada DM Tipe-2 ...................... 54
6.5 Keterbatasan penelitian............................................................. 56

BAB 7 KESIMPULAN DAN SARAN .................................................... 57
7.1 Kesimpulan................................................................. 57
7.2 Saran................................................................. 58

DAFTAR PUSTAKA ................................................................................. 59
LAMPIRAN ..................................................................................................... 67
## DAFTAR GAMBAR

<table>
<thead>
<tr>
<th>Gambar</th>
<th>Judul</th>
<th>Halaman</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gambar 2.1</td>
<td><em>The Egregious Eleven</em></td>
<td>7</td>
</tr>
<tr>
<td>Gambar 2.2</td>
<td>Proses pembentukan lesi aterosklerotik</td>
<td>17</td>
</tr>
<tr>
<td>Gambar 2.3</td>
<td>Mekanisme komplikasi vaskuler DM</td>
<td>19</td>
</tr>
<tr>
<td>Gambar 2.4</td>
<td>Faktor-faktor yang mempengaruhi kekakuan arteri</td>
<td>21</td>
</tr>
<tr>
<td>Gambar 3.1</td>
<td>Kerangka konseptual penelitian</td>
<td>28</td>
</tr>
<tr>
<td>Gambar 4.1</td>
<td>Protokol penelitian hubungan antara NLR dengan kekakuan arteri pada DM tipe-2</td>
<td>38</td>
</tr>
<tr>
<td>Gambar 5.1</td>
<td>Diagram <em>scatter</em> korelasi antara NLR dengan baPWV</td>
<td>46</td>
</tr>
</tbody>
</table>
DAFTAR TABEL

Tabel 2.1 Kriteria diagnosis diabetes mellitus tipe 2 ................................. 8
Tabel 5.1 Karakteristik umum subyek penelitian ....................................... 39
Tabel 5.2 Karakteristik parameter metabolik ............................................ 40
Tabel 5.3 Karakteristik subyek berdasarkan parameter hematologi .......... 41
Tabel 5.4 Hitung Neutrophil-lymphocyte ratio (NLR) pada subyek penelitian ....................................................................................... 42
Tabel 5.5 Nilai baPWV pasien DM tipe-2 .................................................. 44
Tabel 5.6 Korelasi antara NLR dengan kekakuan arteri (baPWV) pasien DM tipe-2 ....................................................................................... 45
Tabel 6.1 Perbandingan karakteristik dasar dan kontrol glikemik pada DiabCare Asia 2012 dengan penelitian ini ......................................... 49
DAFTAR LAMPIRAN

Lampiran 1 Surat Keterangan Kelaikan Etik Penelitian Bersama ............... 67
Lampiran 2 Informasi untuk Mendapatkan Persetujuan Ikut Serta dalam Penelitian (Information for Consent) .................................................. 68
Lampiran 3 Persetujuan Ikut Serta dalam Penelitian (Informed Consent) .... 72
Lampiran 4 Lembar Persetujuan Tindakan Medis ........................................... 73
Lampiran 5 Lembar Pengunduran Diri ............................................................... 74
Lampiran 6 Lembar Pengumpul Data .............................................................. 75
Lampiran 7 Data Subyek Penelitian ................................................................. 77
Lampiran 8 Analisis Statistik Data Penelitian .................................................... 80
### DAFTAR SINGKATAN

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE</td>
<td>Angiotensin Converting Enzyme</td>
</tr>
<tr>
<td>AGE</td>
<td>Advance Glycosilation End Products</td>
</tr>
<tr>
<td>AR</td>
<td>Aldose Reductase</td>
</tr>
<tr>
<td>ARB</td>
<td>Angiotensin Receptor Blocker</td>
</tr>
<tr>
<td>baPWV</td>
<td>Brachial Ankle Pulse Wave Velocity</td>
</tr>
<tr>
<td>cf PWV</td>
<td>Carotid-Femoral Pulse Wave Velocity</td>
</tr>
<tr>
<td>CCB</td>
<td>Calcium Channel Blocker</td>
</tr>
<tr>
<td>CCS</td>
<td>Coronary Calcium Score</td>
</tr>
<tr>
<td>CD</td>
<td>Cluster of Differentiation</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>DAG</td>
<td>Diacyl Glycerol</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>DMT2</td>
<td>Diabetes Mellitus Tipe-2</td>
</tr>
<tr>
<td>eGFR</td>
<td>Estimated Glomerular Filtration Rate</td>
</tr>
<tr>
<td>eNOS</td>
<td>Endothelial Nitric Oxide Synthase</td>
</tr>
<tr>
<td>ET-1</td>
<td>Endothelin-1</td>
</tr>
<tr>
<td>GFAT</td>
<td>Glutamine fructose-6 phosphate amidotransferase</td>
</tr>
<tr>
<td>GLUT</td>
<td>Glucose Transporter</td>
</tr>
<tr>
<td>Hb</td>
<td>Hemoglobin</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Hemoglobin-glikosilat</td>
</tr>
<tr>
<td>HDL</td>
<td>High-density lipoprotein</td>
</tr>
<tr>
<td>HPLC</td>
<td>High Performance Liquid Chromatography</td>
</tr>
</tbody>
</table>
ICAM : Intercellular Adhesion Molecule
IDF : International Diabetes Federation
IL-6 : interleukin-6
IMT : Indeks Massa Tubuh
IRS 1 : Insulin receptor substrate 1
LED : Laju endap darah
LDL : Low-density lipoprotein
PKC : Protein Kinase-C
MDRD : Modification of Diet in Renal Disease
MMP : Matrix Metalloproteinase
MPO : Myeloperoxidase
NADPH : Nicotinamide adenine dinucleotide phosphate
NFKB : Nuclear Factor Kappa Beta
NGSP : National Glycohaemoglobin Standardization Program
NO : Nitric Oxide
NLR : Neutrophil-Lymphocyte Ratio
PAI-1 : Plasminogen Activator Inhibitor-1
PKC : Protein Kinase C
PKV : Penyakit kardiovaskuler
PWV : Pulse Wave Velocity
RAGE : Receptor for AGEs
ROS : Reactive Oxygen Species
SMC : Smooth Muscle Cell
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDD</td>
<td>Tekanan Darah Diastolik</td>
</tr>
<tr>
<td>TDS</td>
<td>Tekanan Darah Sistolik</td>
</tr>
<tr>
<td>TGF-β</td>
<td>Transforming Growth Factor Beta</td>
</tr>
<tr>
<td>TNF</td>
<td>Tumor Necrosis Factor</td>
</tr>
<tr>
<td>TTGO</td>
<td>Tes Toleransi Glukosa Oral</td>
</tr>
<tr>
<td>UKPDS</td>
<td>United Kingdom Prospective Diabetes Study</td>
</tr>
<tr>
<td>VCAM</td>
<td>Vascular Cell Adhesion Molecule</td>
</tr>
</tbody>
</table>