We aimed to evaluate the cancer detection rates of 6-, 10-, 12-core biopsy regimens and the optimal biopsy protocol for prostate cancer diagnosis in patients with renal failure. A total of 122 consecutive patients with renal failure underwent biopsy with age-specific prostate-specific antigen (PSA) levels up to 20 ng/mL. The 12-core biopsy technique (sextant biopsy + lateral base, lateral mid-zone, lateral apex, bilaterally) performed to all patients. Pathology results were examined separately for each sextant, 10-core that exclude parasagittal mid-zones from 12-cores (10a), 10-core that exclude apex zones from 12-cores (10b) and 12-core biopsy regimens. Of 122 patients, 37 (30.3%) were positive for prostate cancer. The cancer detection rates for sextant, 10a, 10b and 12 cores were 17.2%, 29%, 23.7% and 30.7%, respectively. Biopsy techniques of 10a, 10b and 12 cores increased the cancer detection rates by 40%, 27.5% and 43.2% among the sextant technique, respectively. Biopsy techniques of 10a and 12 cores increased the cancer detection rates by 17.1% and 21.6% among 10b biopsy technique, respectively. There were no statistical differences between 12 core and 10a core about cancer detection rate. Adding lateral cores to sextant biopsy improves the cancer detection rates. In our study, 12-core biopsy technique increases the cancer detection rate by 5.4% among 10a core but that was not statistically different. On the other hand, 12-core biopsy technique includes all biopsy regimens. We therefore suggest 12-core biopsy or minimum 10-core strategy incorporating six peripheral biopsies with elevated age-specific PSA levels up to 20 ng/mL in patients with renal failure.